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Causes and Therapy of Anemia

Aleudrin in Bronchial Asthma

Carcinoma of the Lung • Research • The General Practitioner Issue

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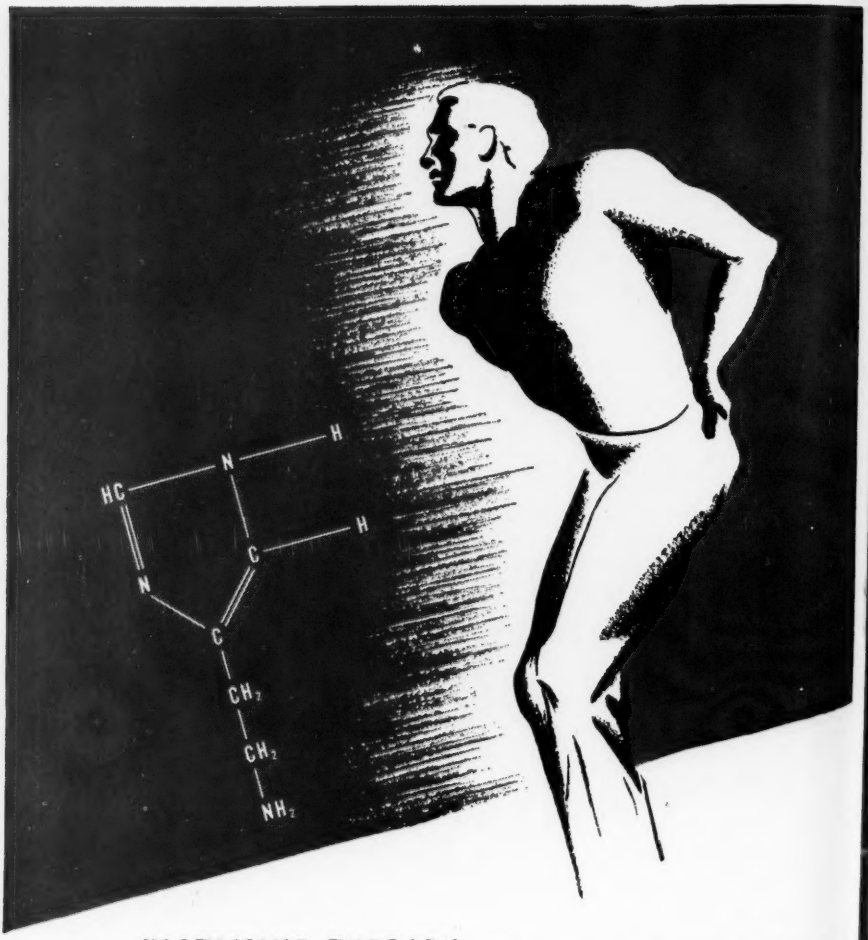

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EDITORIALS

Rationalization of the Lottery

Our terrifying tax structure—income, inheritance and excise—is such that private philanthropy can no longer do justice to our private institutions. Nor can the lottery be looked to at present as a source of funds, as was the case with Harvard and Yale, Philadelphia's Christ Church, and many other of our institutions throughout the eighteenth century; thus the Continental Congress resorted to it in 1777. The people of that day were conditioned against excessive and inequitable taxation; they fought the American Revolution and won their independence on a taxation issue.

But lotteries are now prohibited in all the states and territories of the United States. Meanwhile we see our hospitals collapsing into insolvency.

No question of morals is involved, as gambling in other forms is tolerated, as in the case of games of chance under the most respectable auspices, or even legalized, as in the case of the racetracks; gambling in stocks is of course a commonplace and a vast amount of money passes in the homes of the people.

The government no longer needs the lottery for its public works and other activities, since the tax "take" is so vast. Moreover, the channelling of millions into private lotteries of all kinds would tend to disturb the tax structure itself, hence is taboo; too much revenue would be siphoned from the winnings of the government croupier.

It is true that legalized lotteries *of all types* would divert a stupendous and unconscionable amount of revenue, something which any government, extravagant or non-extravagant, could not be expected to countenance. But lotteries do not have to be rackets and there is no good reason why lotteries in aid of hospitals should not be licensed and applauded. There is hardly any other way today to meet requirements. And legalization of this type of lottery would have a lethal effect upon all forms of illegal gambling.

It is often said that the lottery is the last resort of an impoverished nation. Well, excessive taxation can be impoverishing to the richest of nations.

Insistence upon the type of lottery we have suggested *as a brake* on excessive taxation might carry some appeal to men concerned about governmental extravagance and also about the fate of the voluntary hospital.

Why not move now to rationalize the lottery?

Will the Voluntary Hospital Take Over the Practice of Medicine?

In its report on Hospital Clinic Services, the Special Committee of the Hospital Association of Pennsylvania postulates the voluntary hospital of the future as the center for complete health care to every part of a community, including the ambulant patient. The Committee's favor goes to the diagnostic treatment clinic, rather than the purely diagnostic clinic, for one reason because the latter is not self-supporting. It also discountenances the independent group clinic.

The Committee does not commit itself on the fate of private medical practice under its recommendations. It professes to be against profit seeking on the part of such group clinics as it advocates, while admitting the possibility of notable growth in plant and equipment, including expansion of the bed capacity of the hospital

itself. It speaks in terms of "the growing business of the clinic."

The Committee considers all this to be merely in accordance with the trend of the times.

X-ray of the Sickness Insurance Swindle

In a study made for the National Industrial Conference Board, Dr. Walter Sulzbach warns against the tendency of a social insurance bureaucracy to expand its system beyond the scope originally planned for it; the vested interests of the bureaucracy itself make the bureaucrats "imperialists for their particular departments." Dr. Sulzbach doesn't say so, but the process seems to us much like a cancerous growth. All of which is favored by a fault of the people themselves; having seen billions melt away under wasteful government they have lost their sense for figures and generally lack comprehension of the consequences involved in thriftlessness and reckless budgeting.

Moreover, says Dr. Sulzbach, alleged beneficiaries are fooled; *there is a popular illusion that the employers share in the expenses,* whereas the truth is that "wages would be higher if the employers did not contribute to social insurance."

Dr. Sulzbach's monograph is the second in a series of "Studies in Individual and Collective Security."

A New Challenge

The country-wide nursing experience of the Metropolitan Life Insurance Company in 1925 among its policy holders showed that nearly fifty per cent of the cases were then nursed for the acute and communicable conditions, mostly occurring in early life, with only about five per cent of chronic diseases, conditions typical of advanced life. In 1945 its experience showed a complete reversal, that is, fourteen per cent were cases of acute and communicable conditions, while twenty-eight per cent were nursed for chronic diseases. Here we have a measure of the burden of invalidism at the older ages. The Metropolitan statistician estimates that seventy per cent of our permanently disabled invalids are at ages forty-five or higher and that by the end of the century eighty per cent of invalids will be in this age range.

✚

Promotions and Appointments at Long Island College of Medicine

Seventy-four faculty promotions and fifty-one new appointments to the teaching staff of the Long Island College of Medicine were recently announced by Dr. Jean A. Curran, president of the College. The promotions and appointments were approved at a recent meeting of the Board of Trustees of the Brooklyn medical school.

The new appointments are the first to be made since the College returned to the normal four-year peacetime curriculum. With these additions, the number of men and women engaged in full or part-time training of new doctors has been raised to 418.

Graduate Doctors' Course Authorized

The New York State Board of Regents has authorized the Long Island College of Medicine, Brooklyn, to confer the degree of Doctor of Medical Science.

This is the first full-time, long-term graduate course to be offered by the 87-year-old medical school which in the past has sponsored only a part-time program of graduate training.

Therapeutical Studies in Bronchial Asthma With the Aersols of Aleudrin

Robert Charlier, M.D.

Belgian, Fellow of the British Council

Liége, Belgium

Before dealing with clinical results provided in bronchial asthma by the use of the aerosols of Aleudrin it is necessary to give a brief account of previous experimental researches we carried out during these last few years with several aerosols and so to show how we came to apply such aerosols to the treatment of bronchial asthma.

At first the action on the efficacy of the respiration of a few deep aerosols inhalations (from 20 to 10) was studied on healthy human beings. It was shown[27] that under these circumstances, i.e., after very small doses have been given which do not result in an intra-arterial resorption of the inhaled drugs through the lungs,* such aerosols mostly act locally on the broncho-pulmonary tree. Thus some physiological phenomena occur which can differ widely but are closely dependent on the nature of the nebulized drug.

(a) With some drugs usually regarded as bronchodilators[23,24] such as sympathicotonic compounds, Phenylaminopropan (Benzedrine or Amphetamine), Phenylmethylaminopropan (Pervitin), Ephedrine, Arilin[17], Adrenalin, Aleudrin, Neo-synephrine and also other substances as Cocaine, Novocain, Histamine,[26] there appear simultaneously a decrease of the hourly pulmonary ventilation, an intensive slowing of the respiratory rate, an important increase of the volume of each respiration (as much as 2 liters and more), an increase of CO_2 percentage in expired air together with a fall of the alveolar-CO_2 percentage. These effects induce a decrease of the centesimal value of the dead space (calculated from the data obtained for the CO_2 and O_2 percentages by the analysis of both expired and alveolar airs) and, consequently, a similar rise in the effective ventilation. As the large bronchi are not very extensible, it was theoretically stated that all these changes that are especially important after a few inhalations of aerosols of Aleudrin[24] cannot be ascribed to any dilation of the large bronchi but must be induced by both an increase in the size of the smallest bronchioles (infundibula and atria) and also an opening of some pulmonary areas which are not normally working.

Later on this conclusion was confirmed by direct experimental observations. Of course, some of the pneumodilator aerosols used, chiefly the Aleudrin-aerosols, are able to improve the pulmonary mechanics to such a point that the effective ventilation and the coefficient of utilization of the inspired air (i.e., effective ventilation divided by total ventilation measured), which is normally about 60 per cent, goes up to a value of 90 per cent and in some cases even more. Such improvement of the deep pulmonary ventilation can only be explained by an increase of the lung volume in exertion. Indeed, this was later investigated[28] by means of a direct method, volumetric pneumography, which not only confirmed the pneumodilator action of all sympathomimetic aerosols used (particularly important in the case of Aleudrin)

From the Faculty of Medicine, University of Liége, Belgium.

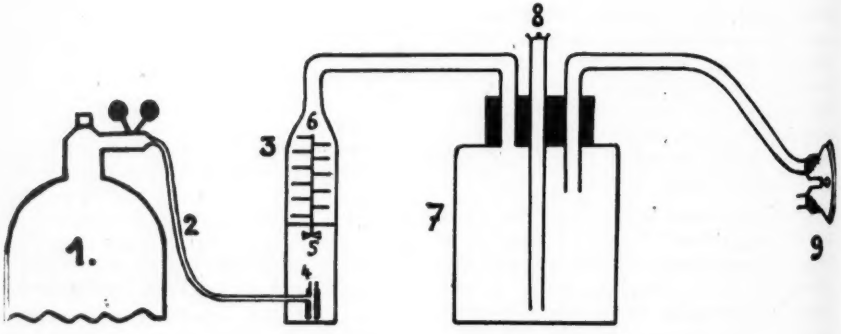
* It is easy to get in both animal and man such transpulmonary resorption when larger dosage is used (19, 20, 21, 24, 25, 27).

but also measured in centimeters the degree of the modifications in the pulmonary volume induced by several aerolized sympathicotonics.[29] Aleudrin was shown to have the strongest pneumodilator effect; far behind are Neo-synephrine and others.

(b) On the contrary, when pneumoconstrictor drugs are aerolized, for example Choline, opposite phenomena are noted. In dogs a real asthmatic paroxysm quickly occurs which involves such respiratory resistance that asphyxia takes place, so that in this case Choline, which is known as an hypotensive drug, regularly produces arterial hypertension due to anoxia. It is easy to get such breathlessness in healthy subjects by inhaling Carbaminocholinaerosols. Here also an experimental asthma crisis takes place with hyperventiltaion and tachypnea; the CO_2 percentage falls in both expired and alveolar airs, the volume of each respiration goes down, while a big increase is noted in the volume of the dead space, the final result being a considerable drop in the respiratory coefficient.[18,23,24] In brief, all these phenomena appear to be quite similar to clinical asthma.[30,43]

The preceding experimental observations led to the evidence that the respiratory effects induced by the pneumodilator aerosols are to be reached in the treatment of asthma where the spasm of the respiratory tract, segmentary or generalized, together with some area of the lungs which does not open freely during inspiration, counteracts the uniform passage of air through the upper respiratory tract into the alveoli.

In order to assess the effectiveness of the pneumodilator aerosols in bronchospasm, experiments were then carried out on several healthy subjects. When after inhaling pneumoconstrictor aerosols and thus getting a severe dyspneic attack the subject is given pneumodilator aerosols all the functional signs of the respiratory distress promptly disappear.[23] In these last conditions of experimental asthma on normal human beings the powerful relaxant action of such aerosols appears to be especially spectacular because with only a few inspirations the paroxysmal dyspnea ceases and the respiratory rate also becomes very slow, in fact, quite similar to that occurring in healthy people who inhale only pneumodilator aerosols without having previously received pneumoconstrictor aerosols. What is more, if after the subject has been freed of the experimental dyspnea crisis by pneumodilator aerosols, attempts are made to renew a paroxysmal attack by giving pneumoconstrictor aerosols again, these are unable to overcome the action of the pneumodilator aerosols and the respiratory movements remain slow and deep.



As on one hand these experimental investigations prove that the pneumodilator aerosols are able to increase greatly the efficacy of the respiration in healthy subjects put in an experimental hyperparasympathicotonic state, and as on the other hand the clinical asthmatic paroxysm finally results in a reduction of the efficacy of the respiration,[30] it was quite natural subsequently to try by means of pneumodilator aerosols to overcome the spasm and to open widely the respiratory tract in patients suffering from bronchial asthma.

So it was briefly reported that[15] when inhaled at the height of an acute attack of asthma aerosols of Ephedrine or Benzedrine involve both slowing and deepening of the thoracic movements, together, as in the healthy subject, with pulmonary hypoventilation and increase in the time of voluntary apnea; there is an almost immediate disappearance of the acute dyspnea, too.

When ultimately Aleudrin was known, preliminary short trials of treatment were undertaken on asthmatic patients, but only on a few people,[22] and evidence immediately appeared of its great superiority in managing bronchial asthma.

After such preliminary observations on asthmatic patients had been done Aleudrin was supplied in sufficient amount to enable us to carry out sustained therapeutical trials on a great many patients suffering from asthma with or without other pulmonary disorders.

The purpose of this communication is to present the clinical results obtained by the nebulization therapy with Aleudrin. The great amount of clinical and therapeutical facts we were led to collect are obviously interesting for the management of bronchial asthma.

To begin with the clinical studies, we must say that the present report does not concern itself with the problems of etiology and pathogenesis of asthma, which have given birth to plenty of investigations, the most recent of which are those of Sanderson,[47] Dellar[31] and Tuft.[52] Present researches were undertaken only from the therapeutical point of view and our sole aim is to report on the valuable results which can be obtained by the treatment.

As already said, we previously reported only some partial observations made on a few individuals and on whom, in order to test only the efficacy of the method during acute attacks of asthma, the treatment was short, irregular and different for each subject from the point of view of the frequency of the inhalations and the concentration of the solution used.[22] On the contrary the treatment given in the present cases is the same for all subjects and is carried out at sufficient length in order to secure complete relief, as described later.

The present studies started five years ago. Until now, 197 asthmatic patients have been treated; all were suffering from bronchial asthma, acute and/or chronic.

We shall now outline the different features of the method and materials.

Treatment and Technic

A.—*The treatment.*

Apparatus. The apparatus used for the present therapeutic purposes is, as far as the technical principles are concerned, similar to that reported elsewhere.[23,24,27] Briefly, it is a big copper atomizer consisting of two essential pieces. First, a powerful steel ejector operates at the bottom of the nebulizer, in the solution; it is connected by a thick rubber tubing with an oxygen tank; the gas delivered at a pressure of 2-3 kgr/cm2 passes freely through the tubing; as the exit of the ejector is very small the solution is sucked up by the oxygen stream so that it is sprayed as a fine suspension. The second piece of the atomizer is a very important one. When issuing from the ejector, only a part of the sprayed solution is really aerolized; in other words, the ejector provides a mist which is in fact a mixture of aerosols and of bigger droplets. It is important to prevent these droplets from entering the bronchi because there would be waste of solution and because they are useless; if breathed in by the patient they are soon arrested and settle in the upper air passages where they are without therapeutic effect for asthma. Therefore the

spray coming out of the ejector is pushed directly to a little propeller (which increases the dispersion of the solution) attached at the bottom of the second piece, which is a dense filter system with baffle plates through which the mist passes, losing the large particles, so that finally only aerosols leave the apparatus. It is noteworthy that thus we always get a very dense mist, extremely thin, absolutely dry. Leaving the atomizer gently, the aerosols come through a large inlet glass tube into a great glass bottle of 10 liters whose cork has an inspiratory valve and an outlet tube leading to a respiratory mask provided with two valves, inspiratory and expiratory. Thus it is quite easy to get proper control of the atomizer's work and the inhalations of the patients.

Drug. Only one drug was used, Aleudrin. It is in fact well known that many times other sympathomimetic drugs have been used as mists in treating asthma, chiefly adrenalin with or without glycerin, combined or not with neo-synephrin* and also ephedrine and benzedrine.[1,2,3,7,11,13,32,33,35,36,38,41,42,45,48,50,53,54] We recently reported that the pneumodilator and antidyspneic effects of those drugs, although beneficial chiefly in aerosols form,[15,18,22,23,24,25,27,28,29] are, as some other spasmolytic drugs, e.g., Phenylmethylaminopropan, Novocain, Sodium nitrite,[23,24] of far less value than those of Aleudrin aerosols.

Aleudrin† is an isopropyladrenalin: C6H3 (OH) 2 - CHOH - CH2 - NHCH (CH3)2. In animals, its relaxant action on bronchospasm is 10 times greater than that of Adrenalin.[39,46,49] Aleudrin is highly pneumodilator in both healthy and asthmatic subjects.[22,24,28,29] Though beneficial in asthma when given by perlingual route or as simple sprays,[6,37,40,44,46,55] it acts very strongly when aerosols are used[24] and quickly abates experimental dyspnea crises induced in healthy subjects by Choline-aerosols.

The solution employed is 0.2 p.cent; very occasionally we were obliged to use larger dosage, 0.3 or 0.4 p.cent, in cases where the initial improvement did not appear sufficient. One must take care to avoid higher dosage because, although the improvement in asthma is not greater with solutions above 0.4 p.cent, transpulmonary resorption of Aleudrin takes place in a high degree[24] and very commonly causes, even in healthy subjects, when a solution of 0.5 p.cent is used, side-effects which are always unpleasant, even dangerous, as tachycardia, palpitation, sudden arterial hypotension, anginal pain, fainting and circulatory collapse, which occur more often in asthmatic patients, in whom they are all the more dangerous as the right heart is frequently the seat of myocarditis.[14] It is obvious that the technique used by some French workers[51] for atomizing Aleudrin does not provide real aerosols, for they never report either side-effects or accidents with the common use of a solution of 1 per cent, which always involves with our technique, even after only three deep inspirations, alarming and prolonged circulatory disorders,[24] induced, as we have reported elsewhere, by an intensive peripheral vasodilatation and also some degree of myocardial tetanus which makes the ventricular chambers unable to empty themselves as they do normally.[12,16] Similar side-effects do not occur except slight tachycardia with the 0.2 p.cent solution.

Inhalations. The technique of the inhalations must allow the aerosols not only to enter deeply into the lungs but also to settle in great amount on the walls of the smallest bronchioles. Such conditions are easily fulfilled when the patient is asked to breathe slowly and deeply and to hold his breath in inspiration for a few seconds; thereafter he expires deeply. Generally speaking, ten consecutive respiratory movements are performed three times with a rest of 3-5 minutes between each of the 3 series. Thus what we call one sitting in-

* Nebulized neosynephrin has been used for asthma by several workers (35, 36, 48) sometimes in association with adrenalin (2, 3), in solutions at 1 to 5 per cent, chiefly when pulmonary secretions are particularly abundant. The results reported were apparently satisfactory.

† Manufactured by C. H. Boehringer Sohn, Ingelheim am Rhein, Germany, and by Frederick Stearns and Company, Detroit, Michigan; the latter's product is known as Isuprel.

cludes 30 respiratory movements. It is easier for patients who are particularly breathless to perform 6 series of 5 respiratory movements. Each sitting takes about 15-20 minutes. Conversely to what Barach[4] thinks, we were able to use this technique in all cases, even in patients at the height of an acute attack. It is a question of will and steadiness from the patient and chiefly of perserverance and advice from the physician. It is very important to take account of all these modalities of the inhalations, for the aerosols have to penetrate deeply and to deposit in the smallest bronchioles, which are the site of spasm and where aerosols act.[8,9,10]

Course of the complete treatment. After performing preliminary clinical studies (not here reported) in order to find out the best method, the length of the treatment and the frequency of the inhalations were set as follows: one sitting every day during 4 weeks, then 3 sittings a week during 4 weeks, followed by 4 weeks again with 2 weekly sittings and finally one sitting per week during one month.

The treatment must be very regular and very strict to achieve striking improvements.

B.—*The patients.*

Rather than presenting detailed case histories for each patient, we preferred to summarize and to classify the patients, chiefly in order to get a better general view of the results.

Four principal tabulations are made, based upon the four following characteristics, respectively the age and sex (Chart 1), the type of dyspnea, the severity of asthma, the dominant eitology of asthma.

CHART I

Tabulation of the Patients according to Age (years) and Sex

Under 20		From 20 to 40		From 40 to 60		Over 60	
M	F	M	F	M	F	M	F
26	11	37	27	55	24	15	2
37		64		79		17	
19%		32.5%		40%		8.5%	

Let us give a few particulars about the terms employed. To get precise information regarding such basic components, it has been found necessary to go through a careful history of the disease and to make a thorough and complete examination of each patient.

Concerning the type of dyspnea (which is arbitrarily chosen as that observed during the last three months before the treatment began), the cases are classified for the purpose of tabulation as four types according to the data estimated from the functional anamnesis (Chart 2).

CHART II

Tabulation of the Patients according to the Type of Dyspnea

Type 1	Type 2	Type 3	Type 4
17	17	76	87
8.5%	8.5%	39%	44%

Type 1: where the dyspnea occurs almost exclusively as paroxysmal attacks, varying in severity and frequency, as often by day as by night; rarely, only slight breathlessness "takes over."

Type 2: also here only paroxysmal attacks but occurring only at bedtime, very often at one or several given moments; in such cases, the attacks are very commonly severe and regular.

Type 3: the patients here listed are afflicted with both chronic asthmatic dyspnea and from time to time acute dyspnea but, functionally speaking, the patients are chiefly complaining of chronic breathlessness.

Type 4: here the subjects are chiefly suffering from chronic dyspnea, almost without (except very rarely) acute attacks. However, it must be borne in mind that even in the patients listed as type 4 at least one acute attack occurred, whatever its severity and the moment of its appearance may have been; very often this attack was produced by emotion, mist—or dust—inhalations, special food or drugs like quinine, acetylsalicylic acid, anesthetics. We excluded patients who were only suffering from other chronic diseases causing dyspnea, as pulmonary emphysema, chronic cardiac insufficiency.

The third kind of tabulation considered is based on the severity of the dyspnea;

four degrees were assumed as slight, mild, serious and severe, according to the severity during the six months preceding examination (Chart 3).

CHART III

Tabulation of the Patients according to the Degree of Dyspnea

Slight	Mild	Serious	Severe
18	126	39	14
9%	64%	20%	7%

Taking into account all the eitological conditions of the patients we finally made a fourth classification according to the dominant etiology of asthma. We chiefly listed chronic bronchitis, digestive disorders (hepatic type), nasal type, bronchitic and hepatic type, bronchitic and nasal type, hepatic and nasal type, anaphylactic type (Chart 4).

CHART IV

*Tabulation of the Patients according to the Etiology of Asthma**

1. Bronchitic asthma	117	60 %
2. Hepatic asthma	29	15 %
3. Nasal asthma	4	2 %
4. Bronchitic and hepatic asthma	4	2 %
5. Bronchitic and nasal asthma	3	1.5%
6. Hepatic and nasal asthma	2	1 %
7. Anaphylactic asthma	4	2 %
8. Not determined	34	17 %

* It is worth noting that all the main causes of bronchial asthma were encountered and that chronic bronchitis is, as commonly known, by far the most frequent with 63.5 per cent of cases (categories 1, 4 and 5).

Besides, we also noted carefully the frequency of some pathological features (Chart 5) which are clinically interesting, as: personal or familial tuberculous antecedents, slight liver insufficiency, chronic heart insufficiency, pulmonary emphysema, subjective complaints due to long standing arterial hypertension; we also listed people who had worked several years as coal miners (pitmen).

CHART V

Tabulation of Pathological Features added for the 197 Patients

Tuberculous antecedents	50	25 %
Slight liver insufficiency	10	5 %
Coal miners	14	7 %
Chronic heart insufficiency	20	10 %
Pulmonary emphysema	21	10.6%
Long standing arterial hypertension	7	3.5%

Results

Let us remember that the present problem is to be defined clearly, in other words that the aim of the study is to explore and to estimate not the early response to Aleudrin-aerosols but only the final benefit that can be given when a complete course of treatment is administered. Of course, the immediate action of such inhalations has already been reported elsewhere:[22] in brief, after only one sitting, there always occurs an immediate pneumodilator effect characterized by a considerable slowing down of respiratory rate, deepening of thoracic movements, increase of vital capacity and of the length of voluntary apnea, a disappearance of dyspnea and a feeling of well being; in fact, all the attacks are stopped by Aleudrin-aerosols even when other drugs such as adrenalin or morphine have failed.

To come to the real purpose of our studies, i.e., the actual benefit derived for asthma from a complete treatment with Aleudrin-aerosols, it is obvious that the degree of improvement varies with each patient. Thus it was found necessary to consider various degrees in improvement. Therefore we have divided the patients into four categories.

Category 1: includes cases displaying striking improvement, more than 90 p.cent; here is lasting disappearance of asthma whether of paroxysmal attacks in patients who previously suffered from such paroxysms frequently, or of chronic dyspnea and minor asthmatic attacks which used to occur with surprising easiness on various occasions such as small efforts, digestive disturbances, sudden changes in external temperature, removal from one area to another, exposure to mist or dusts. By "lasting disappearance"

of asthma is meant a period of at least one year but more often of three or more years.

Category 2: the patients are greatly improved, let us say 75 p.cent; they are relieved of chronic or acute dyspnea but when meeting any of the different factors quoted above some breathlessness appears which is far less disturbing than before and is always easily overcome by minor sedative measures.

Category 3: the patients claim 50 p.cent relief of symptoms; the acute attacks are far less important in frequency, severity and duration or the chronic dyspnea is much lessened but not entirely removed. It seems that in this category the dyspnea, whether acute or chronic, is particularly difficult to remove when patients do not take care to avoid the interference of the above-mentioned "asthmatogen" factors; chiefly here the modus vivendi of asthmatic patients, of which we talk later on, must be recommended. Nevertheless, when dyspnea recurs in those instances breathlessness is always less important and frequent than prior to treatment. The patients obviously retain benefit obtained from Aleudrin-aerosols.

Category 4: moderate improvement of about 25 p.cent; the functional relaxation is often important but it occurs after a large number of sittings only and is generally insufficient anyway; in such patients, chiefly the nightly dyspnea is lessened. Here it is advisable to use Aleudrin solutions of 0.3 or 0.4 p.cent, which are able to increase improvement.

According to the preceding considerations, we classify in chart 6 the 197 patients managed.

It seems quite useless to dwell at large on the results reported. Summarizing on one hand the cases that respond favorably (four first categories in chart 6) and on the other hand the patients where the treatment has failed (two last categories), it appears that 175 patients or 88.5 p.cent have improved and 22 cases or 11.5 p.cent have not.

It is necessary to stress the following point: if the physician wishes to reach the highest level in improvement the asthmatic patients must in the beginning of the therapy have one daily sitting so that they are permanently under the influence of the action of Aleudrin-aerosols; only after that, as the clinical improvement gradually increases, one can progressively space the sittings; this assumption is true for all patients—even for the mildest cases. In these last cases one can use shorter periods of treatment only so that instead of having four periods of four weeks one can have four periods of three weeks, even of two weeks, in the very mild cases, but spacing of the sittings from the beginning of the treatment is always contraindicated.

CHART VI
Clinical Results obtained by Aleudrin-aerosols in the 197 Patients

Degree of Improvement	Number	%
Category 1 or more than 90% improvement	20	10
Category 2 or 75% improvement	93	47
Category 3 or 50% improvement	49	25
Category 4 or 25% improvement	13	6.5
Category 5 or no improvement	19	10
Category 6 or aggravation in spite of treatment	3	1.5

Observations

Above the very satisfactory clinical results provided by the Aleudrin-aerosols in the 197 patients one is lead to stress other important clinical facts.

As already said, the improvement induced is generally only temporary, but this does not exclude many complete remissions, for twelve patients, even severe cases, have been free from asthma for two to five years after treatment. But it is noteworthy that when the dyspnea again occurs after a complete therapeutic course the severity of the distress is far less because, it can be assumed, some pneumodilation remains together with improvement in the respiratory dynamics. It is of course doubtless that performing frequent voluntary deep and slow lung ventilation leads to a re-education of the respiration which improves for a long time the respiratory

status of such patients. When dyspnea reappears a new pneumodilator "cure" is quite useful and acts as successfully as the first one.

The general status is greatly improved, too, and we were very often impressed by its high degree: appetite greatly increased, digestive tolerance for "asthmatogen" food, weight going up to 12 or 15 p.cent (even in the case of patients previously in satisfactory general state), increase in effort capacity, general feeling of well being.

The action of Aleudrin-aerosols results not only in quickly releasing the bronchospasm but also in all patients the sputum becomes almost immediately thinner, the expectoration quite easy; this expectorant power of such aerosols is important and lasting and much greater than that of the usual expectorant drugs, as already stated by several workers who only used adrenalin with or without neo-synephrin.[1,2,3,11,13,35,36,41,42,45,48,54] Furthermore, with several inhalation sittings expectoration is gradually reduced and clearing of sibilant râles takes place. Finally, the patients often become entirely sputum-free.

One further benefit derived from such Aleudrin-aerosols in the general therapy of asthma is that they prove to be of more value than adrenalin and morphine in releasing the respiratory spasm during an acute attack, even when these last drugs have not succeeded. One such case has been reported.[22] Among the 197 patients we had the opportunity to confirm what had already become almost uncontrovertible. Many times patients who were unresponsive to repeated routine measures like adrenalin or compounds with adrenalin, such as ephedrine, pituitrin, atropine, morphine, have not only been relieved of acute attacks as soon as given Aleudrin-aerosols but after a complete treatment a truly remarkable clinical recovery has also been noted. During such acute attack patients are of course generally unable to perform deep inspirations immediately, but as soon as a few aerosols are entering into the respiratory tract they result in progressive freedom from spasm, the dyspnea is subsequently lessened so that patients are able to breathe more deeply and in so doing to take in more aerosols, and so forth. Generally within twenty minutes the paroxysm is over. In certain severe cases, particularly in the beginning of the treatment, it is sometimes useful to perform longer sittings with for instance 60 to 100 respiratory movements.

Aerosols of atropine prior to the Aleudrin-aerosols at each sitting were recommended for the asthmatic patients in whom dyspnea is accompanied by great bronchosecretion.[15] But we were unable to confirm this fact. Conversely we often saw that giving such patients aerosols of atropine resulted in supplementary respiratory discomfort and that is quite understandable. In fact coughing is the only means for them to get rid of the abundant secretions which are one cause of dyspnea and so to induce a relative release from dyspnea. If cough is neutralized by atropine-aerosols (and it must be said that it has never been proved that the atropine-aerosols were able to make the secretion stop), then one notes only a supplementary obstruction in the respiratory tract. All our hypersecretant patients got as much profit out of the Aleudrin-aerosols solely as those having no secretions of bronchitis. But in asthmatic patients who are suffering at the same time from chronic bronchitis with abundant expectoration the pulmonary reaction appears to be different: instead of a feeling of immediate relief, patients generally have to wait for one or two weeks before claiming improvement. From the first day of the treatment, the sputum becomes thinner and more abundant; the cough increases but so does the expectoration, which becomes easy. During a few days considerable expectoration takes place so that the patient really empties his lungs. Then the râles gradually disappear, while production of secretions and at the same time cough and dyspnea quickly and greatly decrease.

Generally speaking, the improvement induced in asthma by Aleudrin-aerosols is very rapid and at first very important in the patients who suffering from severe and repeated acute attacks. We often met people, chiefly young, suffering severely who required for instance two to four in-

jections of adrenalin and sedatives every night and in whom the first inhalation sitting was followed by an uninterrupted sleep without the slightest dyspnea.

It seems that people with tuberculous antecedents are particularly amenable to treatment by Aleudrin-aerosols. Generally they get an early and maximal improvement.

The asthmatic patients having also pulmonary emphysema seem to be those who show the smallest improvement.

Discussion

All the good clinical results reported here with the use of Aleudrin-areosols in 197 asthmatic patients are without doubt attributable specifically to the Aleudrin-aerosols and are the results of this treatment alone. Of course, on the one hand the improvements noted always started as soon as the treatment was begun. Up to that moment all the patients were either in status quo or gradually becoming worse. So we can exclude the occurrence of more or less long spontaneous remissions as may commonly happen during the life of an asthmatic patient. On the other hand, as we intended above all to test the efficacy in asthma of the Aleudrin-aerosols, we rejected all the other antiasthmatic measures in contrast with other workers who, with a view to apply a complete treatment, use sympathicotonic mists (chiefly adrenalin) together with various other measures.[5,48] To this end, before starting Aleudrin-aerosols, we first made the patients stop any antidyspneic therapy, both fundamental therapeutics such as all forms of vaccinotherapy, desensitization, massive D vitaminotherapy with calcium, often used in our country,[34] and the symptomatic drugs. As to those last drugs, it is surprising how frequently and how quickly the patients receiving Aleudrin-aerosols stop using such medications. They do not need them any longer. Besides, as soon as aerosols start many patients give up the soporifics which were necessary for them to find a few hours relative sleep at bedtime with some respiratory relaxation. Aleudrin-aerosols not only make the use of barbiturates as somnifacients useless for the asthmatic patients but they also induce a normal sleep.

Only one exception to the general therapeutic rule need be noted. We used digitalis in maintenance dosage per os (generally 1 mg. digitaline daily for five or ten days) in the twenty patients who had also chronic heart insufficiency.

Practice showed us that it is often convenient, in certain patients, to order them a settled modus vivendi where the basic components are: (a) an alimentary hygiene chiefly consisting in the fact that the supper must always be very light and taken at least two hours before sleep; the relevant recent observation of Sanderson[47] on this subject completely agree with it. We recommend only toast, fresh butter, very ripe fruit, marmalade, weak coffee with sugar; nothing more. It is obvious that for the asthmatic patients suffering from liver insufficiency one must avoid all food which is known by the patient to occasion digestive troubles and dyspnea. Generally chocolate, cabbages, crustacea, sometimes eggs and pork, seldom milk and feculents, are meant. (b) In the patients who are particularly unmanageable, for the maximal improvement by Aleudrin-aerosols, chiefly in asthmatics with severe nightly acute attacks, in whom minor respiratory troubles are persisting, it must always be borne in mind that a complete removal from bedroom and bed can really round off the effects of Aleudrin-aerosols. In two subjects who were greatly improved by aerosols but who said they still had minor nocturnal attacks we advised this course and we saw the complete relief of asthma. (c) It is also important to avoid colds, which are, as well known, often the cause of attacks, chiefly in asthma with chronic bronchitis,[31] and especially to keep the feet warm.

Conclusions

The present clinical study, confined to the therapeutical effects of the aerosols of Aleudrin in 197 patients suffering from bronchial asthma, shows that if the treatment is instituted with regularity and in a complete course according to settled rules, one can effect clinical improvement often in a very high degree in almost all subjects treated.

The chief evidence derived from this report is that the success of the Aleudrin-aerosol therapy here used depends on four factors:

1) the use of aerosols, which implies the employment of an appropriate apparatus;
2) the use of the most powerful pneumodilator drug so far known, Aleudrin;
3) the technique of the inhalations performed by the patients;
4) the regularity and intensiveness of the complete treatment.

From several observations made by the patients themselves about the efficacy of different therapeutical means they had used, it seems that Aleudrin-aerosols prove superior to the other therapeutic agents chiefly in the case of patients with whom other measures have failed.

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Anemia, A Review of Its Causes and Therapy

Presented herein is a summary of the various types of anemia, symptoms and effective therapy designed as a time-saving refresher for the busy practitioner. Reprints available.

Considerable research in recent years has been devoted to hematology, a branch of medicine devoted to the study of the blood. The functions of the blood are:

1. Respiratory
2. Nutritive
3. Excretory
4. Essential in osmosis and maintenance of water balance.
5. Essential to the maintenance of body temperature.
6. Protection and defense of the body from injury by various agents.

Composition of Blood

The blood is composed of two main parts, the cells and the plasma. The plasma is the liquid portion in which the cells are suspended. The cells include the red or erythrocytes, the white or leukocytes and the platelets or thrombocytes. The plasma is made up of 91 to 92 per cent water and 8 to 9 per cent solids. Serum albumin, serum globulin and fibrinogen (all proteins) constitute 7 per cent. Inorganic constituents which include sodium, calcium, magnesium, potassium, phosphorus and others make up 0.9 per cent. The organic constituents other than the proteins mentioned include such nonprotein nitrogenous materials as urea, uric acid, xanthine, hypoxanthine, creatine, creatinine, ammonia and amino acids; neutral fats; phospholipids; cholesterol; and glucose. Included in the solids are the internal secretions, antibodies and enzymes such as the amylases, proteases, lipases, esterases and others.

Blood Plasma

The blood plasma carries a small quantity of dissolved oxygen which is available to the body cells but this is insufficient for normal use. A man who weighs 150 pounds and who does moderately hard work uses 750 liters of oxygen in 24 hours. The hemoglobin in the red blood cells carries practically all of this oxygen. In order to supply sufficient oxygen from the plasma it would require tremendous quantities of plasma.

Red Blood Cell

The normal, human, red blood cell is disc-shaped and is thinner in the center than on the edges. This shape appears to provide the greatest amount of surface for absorption of oxygen and to allow for rapid and equal diffusion to the interior of the cell. The total surface area of all the red blood cells of the body represents about fifteen hundred times the surface of the body. The cell is nonliving, non-nucleated, does not consume any appreciable quantity of oxygen, and averages about 7.5 μ in diameter, 1 μ thick in the center and 2 to 2.4 μ at the thickest points. A change of the acid-base balance of the blood toward the acid side causes an increase in diameter, thus in venous blood the cells are slightly larger. Muscular exercise also increases the diameter. Forced breathing causes the acid-base balance to shift toward the alkaline side and decreases the diameter of the cell.

The outer membrane of the red blood cell is made up of protein and the lipid materials, lecithin and cholesterol. The inside of the cell consists of a spongelike stroma, the meshes of which hold the hemoglobin. The outer membrane normally is easily permeated by water, urea and various salts in solution.

Origin of Red Blood Cells

There are two theories advanced as to the origin of the blood cells. One is of

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the opinion that all types come from one primitive free cell or stem cell whereas the other theory advanced is that there are two distinct types of stem cell. The first theory appears to have more evidence in its favor. The hemopoietic function of the liver and spleen before birth is taken over after birth by the bone marrow which then produces the erythrocytes, granular leukocytes, blood platelets and possibly some of the lymphocytes. However, the lymphoid tissues assume responsibility for the latter. In the bone marrow is a closed vascular system with an endothelial lining from which the erythrocytes are developed. The leukocytes and platelets are formed outside of this endothelial lining. The bone marrow contains reticulo-endothelial cells such as are present in the liver and spleen and other cells capable of forming erythrocytes are present in the endothelium of its sinuses and intersinusoidal capillaries. In certain conditions these cells may destroy as well as form erythrocytes.

Blood Forming Function

The hemopoietic or blood forming function is thus thought to be in the red marrow which is located in the ends of the shafts of the long bones such as the femur and humerus, and to a somewhat greater extent in the skull, sternum, vertebrae and ribs. The yellow marrow composed of connective tissue and fat normally makes up the greater portion of the marrow. However, it still possesses the essential reticular structure of hemopoietic tissue and thus in pernicious anemia changes into red marrow. In aplastic anemia it increases at the expense of the red marrow. The red marrow is in predominance in the infant and is gradually replaced by the yellow in the adult. Hemolysis, hemorrhage or reduced oxygen tension serve as stimulants to the bone marrow to increase its activity which results in increased numbers of red cells released into the circulation. A rapid rise in red cell count as a result of acclimatization to high altitudes is believed to occur as a result of release of red cells from reservoirs such as the spleen.

New red cells are formed by mitotic division. Before they reach full maturity they pass through a number of stages which can be definitely recognized.[1] The first is the reticular cell from which is formed the hemocytoblast. This hemocytoblast divides into two daughter cells called basophilic erythroblasts. They contain no hemoglobin and are deeply stained by basic dyes. The next stage is the formation of large cells known as polychromatophil erythroblasts which contain a large, round and frequently vesicular nucleus. Basophilic material and traces of hemoglobin are found in the cytoplasm. As the cells mature the concentration of hemoglobin increases. The erythroblasts stain with both acid and basic dyes due to the presence of basophilic material and the acidophilic hemoglobin. This is known as polychromasia or dual staining. As the cells lose the basophilic material in maturity and pass from the erythroblastic stage this property is lost. Nearing the mature erythrocyte the cell is known as a normoblast. It is very close to the mature cell in size and hemoglobin content but retains the nucleus. Finally the nucleus is extruded from the cell and the young mature form is sent into the circulation. At this stage it is known as a reticulocyte since the cytoplasm is still finely basophilically reticulated. Usually the red blood cells gain full maturity before entering the circulation. The stages of development of red blood cells can be studied by means of marrow smears obtained through sternal puncture. This is also a means of studying marrow activity. The antianemia factor which is carried from the liver to the bone marrow is necessary for the production of red blood cells by the latter. In normal healthy tissues the antianemia factor is present in sufficient quantity to provide adequate activity of the bone marrow to replace the used red cells lost from circulation. This antianemia factor is missing in pernicious anemia, particularly. In such cases a shift to the left or a preponderance of the more primitive forms may be present.

Red Cell Life Span

The normal red cell count in healthy

women is approximately 4,900,000 per cu. mm. and in men 5,400,000 per cu. mm. The average figure used in a majority of cases is 5,000,000 per cu. mm.[2] As stated previously the count increases with change in altitude (low to high) as well as with other factors such as muscular exercise, emotional states and increased external temperature. Although the count is generally fairly constant and new cells are always present in process of production it follows that there is a constant destruction or loss of red blood cells. The life-span of the erythrocyte extends anywhere from 25 to 50 and in some cases to 100 days. The red cells are subjected to considerable stress and strain as they pass through the circulatory system so that they gradually begin to undergo fragmentation. Thus as the old, worn out cells pass through the liver or the spleen they are removed from the circulation and destroyed. In addition to the liberation of the hemoglobin and the splitting off of its iron, a bile pigment known as bilirubin is formed. The bilirubin is transported into the intestinal tract by way of the bile.

The stresses and strains to which the red blood cells are subjected include: (1) changes in osmotic pressure which in turn affect the tension of the membrane; (2) contact with other red blood cells and the walls of the blood vessels: (3) the high velocity and pressure with which they are sent from the heart; (4) the many openings through which they are forced are too small to permit freedom of passage. Calculations have revealed that some ten million red blood cells are removed from the circulation every second. Destruction of the red cells causes a liberation of approximately 25 Gm. of hemoglobin, the quantity normally present in 160 cc. of blood. This amount of hemoglobin contains approximately 85 mg. of iron. Since the total blood volume of 5.5 to 6 liters contains approximately 950 Gm. of hemoglobin (14 to 16 Gm. per 100 ml. of whole blood) which in turn contains 3.2 Gm. of iron, this quantity can be spared but it is indicative of a considerable turnover of the iron-containing pigments.[3]

The values in humans vary slightly dependent upon age, sex and the method of determination.

White Cells, Platelets

The white cells contain no hemoglobin and possess a well-formed nucleus. They measure 8 to 15 μ in diameter and are not so numerous as red cells. Children have more white cells than adults. The lymphocytes and monocytes have a single nucleus and clear, nongranular cytoplasm. The granulocytes have a lobed nucleus and the cytoplasm has fine chromophil granules.

The white cells not only provide the body's defense against micro-organisms, but can also be stimulated nonspecifically as by milk injections. Normally they are present in numbers of 5000 to 9000 per cu. mm. of blood.

The platelets are non-nucleated fragments of protoplasm containing two types of granules. They are about one-third as large as the red cells (2.5 μ in diameter) and normally there are about 200,000 to 400,000 per cu. mm. Their function is to disintegrate and liberate thromboplastin necessary in the formation of the blood clot.[1]

Origin of Granulocytes, Platelets, Lymphocytes and Monocytes

Granulocytes and platelets also originate in the bone marrow. The first stage of the former is the myeloblast. They are considered of extravascular origin and upon acquiring motility pass into the marrow vessels. From the myeloblast are formed three types of granulocytes. The cytoplasm begins to show presence of granules and becomes less basophilic. There are four stages during which the cells are known as myelocytes. They are differentiated by increasing numbers of granules and by the shape of the nucleus. In the first three the nucleus is oval and nonlobulated but becomes indented in the fourth stage. In this stage the typical ameboid movement begins. Finally the nucleus becomes deeply indented and the young leukocyte is passed into the circulation. It can no longer divide or grow.

The marrow contains approximately three times as many leukocytic elements as red cell elements but the blood has a ratio of about 1 to 600 probably due to the greater mortality of the former. In order to replace them hematopoietic activity must be increased.

The platelets or thromobcytes are believed to originate from the megakaryocytes (giant cells) in the marrow. They possess an ameboid movement and an irregular, ring-shaped nucleus. The number of platelets in the circulation appears to be influenced by the number of these cells in the marrow.

The lymphocyte comes from a large lymphocyte or hemocytoblast, (closely resembling the myeloblast) present in the lymphoid tissue in the germ centers. These germ centers are located in the central areas of the follicles. The hemocytoblast is also known as the lymphoblast. Passing through various stages of division of cells the lymphocyte is finally produced.

The monocytes are believed to originate either from the lymphocytes in the spleen or from the histiocytes of the spleen and bone marrow. This has not been definitely settled.[1]

Hemoglobin

Hemoglobin is the red coloring matter of the blood. It is a readily crystallizable conjugated protein which consists chiefly of a globin fraction (a colorless protein making up about 96 per cent of the molecule) and an iron-containing pigment (a nonprotein group belonging to the porphyrin class). When the osmotic pressure is determined or the sediment from ultracentrifugation studied the molecular weight of hemoglobin is observed to be approximately 67,000. From this figure it has been calculated that the molecule contains 4 atoms of iron (Fe).[3]

Hemoglobin Formation

Hemoglobin is formed in the long and flat bones of the body as a chief constituent of the red blood cells. In order for it to be synthesized amino acid precursors of the protein globin and iron are necessary in the diet. Some iron is obtained from the normal destruction of red cells. Traces of copper as a catalyst are necessary for the conversion of the inorganic iron. The liver of the embryo plays an important part in red cell formation and hemoglobin synthesis and it is possible that this function is retained to some extent in the adult although the bone marrow is chiefly responsible.[3] It is thought that elderly people experience difficulty in reforming blood which is lost due to blood disease or hemorrhage because so much of the active red marrow is replaced by depositions of fat. Age is an influential factor in the quantity and quality of red marrow.

Oxygen Transfer

Hemoglobin possesses the property of rapidly and reversibly combining with oxygen. For purposes of simplicity this reaction is written as follows:

$$Hb + O_2 = HbO_2$$

Hemoglobin Oxyhemoglobin

If conditions are at an optimum 1 Gm. of hemoglobin is capable of combining with 1.36 ml. of oxygen. This combination is not strictly an oxidation process since the iron in both hemoglobin and oxyhemoglobin is in the ferrous state. Normal blood is believed to contain about 5 per cent of its iron in a form which cannot combine with oxygen.[2]

Oxyhemoglobin is comparatively stable so long as there is sufficient oxygen present to prevent the reaction from reversing. Thus the relative amounts of hemoglobin and oxyhemoglobin in the blood will depend upon the quantity of oxygen present. This concentration of oxygen is dependent upon the oxygen tension of the red cells which in turn is dependent upon that of the plasma. Oxygen freely diffuses through the membrane of the red cell.

From 95 to 100 per cent of the blood is saturated with oxygen and thus practically all of the hemoglobin is oxygenated when the blood is in equilibrium with ordinary room air or with the alveolar air of the lungs. The oxygen tension in ordinary room air is about 150 mm. Hg and in the alveolar air of the lungs about 90 to 100 mm. Hg.[3] The tissues are constantly in demand of oxygen which they

obtain by diffusion of the oxygen from the plasma into the tissue fluids. Thus the plasma oxygen tension is reduced and at this point venous blood is 50 to 75 per cent saturated with oxygen. As the blood under lower oxygen pressure passes through the pulmonary capillaries the hemoglobin is exposed to the higher pressure of the lungs and is resaturated. After resaturation the blood goes back to the heart and then into the arteries and thence into the capillaries.

Various factors influence the rapidity and degree of exhaustion of oxygen from the hemoglobin by the tissues. If the reaction of the tissue fluids swerves towards the acid side due to a rise in the temperature of the tissues as a result of a release of carbon dioxide and lactic acid during exercise or course of a fever the hemoglobin releases oxygen more rapidly than normally. More oxygen is consumed when the tissues are more active.

Increased requirements are met by various means such as increased respiration; more oxygenation; more exhalation of carbon dioxide; an increase in the total amount of blood sent to the tissues; or by a more complete exhaustion of the oxygen from the blood.

The normal blood picture shows an erythrocyte count of 4,500,000 to 5,000,000 which may vary to some extent. The erythrocyte volume is about 42 cc. per 100 cc. of blood. The hemoglobin value is 90 to 100 per cent or 12.5 to 17 Gm. per 100 cc. (3 Gm. per million red cells). The color index is 0.9 to 1.0 and the volume index is 1. The total number of leukocytes varies from 5,000 to 10,000 with an average of 7,000 to 8,000. The platelet count is 200,000 to 400,000. The white cell picture is as follows: the lymphocytes are present to the extent of 20-25 per cent and the large 5-8 per cent with a total of 1,000 to 4,000; monocytes are usually not seen although there may be about 2 per cent; the neutrophil total is 3,000 to 7,000 making up about 60-70 per cent; eosinophils (total 50-300) constitute 1-4 per cent; and the basophils (total 0-100) make up 0.5-2 per cent.

The red cells show a sedimentation rate of less than 0.35 mm. per minute and less than 15 mm. per hour. A test of erythrocyte fragility shows that hemolysis begins in 0.42 per cent sodium chloride solution and is complete in 0.32 per cent solution. Hematocrit determination shows 40 to 48 per cent cells. Reticulocytes make up 0.1 to 1.0 per cent of erythrocytes.

Clot retraction is complete in 1 to 2 hours. Bleeding time is less than 4½ minutes and coagulation time varies from 2 to 10 minutes dependent upon the method of determination. The van den Bergh test for bilirubin shows the following results: direct, 0.4 mg. per 100 cc.; and indirect, toal, 0.7 mg. per 100 cc. The icterus index is 1 to 5.[4, 5, 6]

Definition of Anemia

Anemia is defined as a condition in which the blood is deficient either in quality or in the number of red blood cells or in the quantity of hemoglobin. This in turn decreases the ability of the blood to combine with and carry oxygen to the tissues.

Classification of Anemias

There have been many different classifications of anemia published. Earliest methods simply termed them primary and secondary anemias. This has been considered erroneous since all anemias are believed to result from some basic disorder and therefore, are secondary.[7] Ottenburg has divided the anemias into three major groups as follows: (a) Deficiencies among which are included iron deficiencies, anti-pernicious-anemia principle deficiencies and nutritional deficiencies; (b) Injury to the bloodmaking organs to which class belong those caused by toxic destruction of the marrow, mechanical replacement of the marrow and interference with blood regeneration at some intermediate stage; (c) disintegration of the blood or hemolysis which may occur as a result of hereditary defects of the red blood cells themselves or by toxic destruction of the blood.

Anemias are also differentiated according to color index or hemoglobin content or the cell volume and diameter,[8] According to this classification the first group is

termed hyperchromic macrocytic anemias to which belong the anemias caused by deficiency of the antipernicious-anemia principle from the liver. This group includes pernicious anemia, sprue, pellagra, pernicious anemia of pregnancy, infestation with fish tapeworm, the rare gastrectomy anemia, chronic obstruction of the small intestine, extensive diffuse liver disease, goat's milk anemia, multiple myeloma, leukemias, erythroleukoblastosis and Cooley's anemia. The normocytic anemias result from many causes and require exacting diagnosis. In this group are included anemias resulting from hemorrhages, blood destruction, sickle cell anemia, familial hemolytic icterus, myelophthisic anemias, splenomegalic anemias, anemias associated with deficiency diseases and those dut to infection, and the aplastic anemias. The third group known as the hypochromic microcytic anemias are caused by deficiencies in the factors responsible for hemoglobin formation and include chronic hemorrhage, idiopathic hypochromic anemia and hypochromic anemia from dietary deficiency.

Diagnosis

Careful diagnosis of anemias is extremely important. The history of the patient should be taken into consideration. A general physical examination as well as the usual laboratory tests should be made. The laboratory tests of course will show the status of the blood elements and serve to confirm the diagnosis. From the history can be ascertained any family record of anemia, jaundice or related conditions; the diet and appearance of any symptoms. The physical examination will of course reveal many valuable indications.

Hyperchromic Macrocytic Anemias
Pernicious Anemia

Pernicious anemia is a disease, chronic in nature, which is caused by a deficiency of a certain factor necessary for erythrocyte formation and maturation.

The blood picture in pernicious anemia is helpful in diagnosis.[5, 9] Classified as a hyperchromic macrocytic anemia the total quantity of hemoglobin is reduced but the individual red blood cells are well filled. The erythrocyte volume is reduced and the count reduced sometimes considerably below 2,000,000. The color index is high. Plasma volume varies but toal blood volume is reduced. The leukocyte count is approximately 5,000 to 6,000 but may fall to 1,000. The polynuclear percentage may remain normal. Leukopenia occurs and eosinophilia is fairly common. The platelet count may be reduced particularly in untreated cases. The red blood cells are chiefly macrocytic and the mean corpuscular volume is large. In untreated cases anisocytosis and poikilocytosis may occur. The nucleated forms increase in number with megaloblasts predominating. Plasma pigments are usually increased and show a positive indirect van den Bergh reaction. Diagnosis should be definite before any treatment is begun since therapy exerts a modifying effect on the blood picture.

Hypoprothrombinemia may occur but should not be treated with vitamin K. Bleeding time may be increased and the clot retraction delayed with a normal coagulation rate in cases where the platelet count is greatly reduced.

The active bone marrow is increased in quantity in the very anemic case. The megaloblasts or stem cells are hyperplastic and many show evidence of mitosis.

Pernicious anemia is characterized by the fact that unless adequate therapy is instituted it will proceed alternately with remission and relapse until death occurs.[10] In the periods of remission many of the characteristic symptoms and diagnostic signs return to normal.

Symptoms

The onset of pernicious anemia is insidious and is characterized by achlorhydria, fatigability, numbness, weakness and faintness, tingling and stiffness, nausea, headache, dyspnea, dizziness, pallor, palpitation, diarrhea, abdominal pain, loss of weight, gastro-intestinal and neurologic disturbances, and sore tongue.[5, 6] The neurologic disturbances include numbness and tingling of the extremities, difficulty in walking, stumbling in the dark, urinary

incontinence, headache and psychic disturbances.[9]

Since achlorhydria is more constantly present than other symptoms gastric analysis is valuable in diagnosis. Years may elapse between the appearance of achlorhydria and a change in the blood picture.[11]

As previously stated pernicious anemia is the result of a deficiency in the factor responsible for formation and maturation of the erythrocytes. This factor is known under various names such as the antipernicious anemia principle, the erythrocyte maturing factor, the hematopoietic principle and others. Castle, some years ago, observed that a constituent of the gastric juice which was named the intrinsic factor reacted with some compound in the diet called the extrinsic factor which reaction in turn released the antipernicious anemia principle in the gastrointestinal tract. This principle, by means of the portal circulation, passes into the liver where it is further elaborated and then stored. When there is a deficiency in the bone marrow the liver liberates the antipernicious anemia principle which in turn allows the normal processes to proceed and the erythrocytes to mature. There are various factors which lead to the development of pernicious anemia. They are as follows: the diet may be lacking in protein; the stomach may not properly produce the intrinsic factor; the antipernicious anemia factor may be lost from the body due to ineffective absorption from the intestines, diarrhea extending over a period of time or a deficiency on the part of the liver to store properly the principle and make it available when needed.[7]

Therapy

Observation that patients with pernicious anemia improved upon ingestion of whole liver led to the preparation of an extract containing the active principle. Further work on this extract finally resulted in a highly concentrated preparation. Standards for this product and other preparations used for the treatment of addisonian pernicious anemia have been established by the United States Pharmacopoeia Anti-anemia Preparations Advisory Board. A U.S.P. unit of an antianemic substance is that amount of an otherwise acceptable product which produces, when administered daily, clinical and hematopoietic responses in addisonian pernicious anemia that are considered by the Board to be satisfactory. The label must bear a sttaement of the average dose of the product. It must be stated in terms of the quantity which provides administration at the rate of not less than 1 U.S.P. unit a day whether given daily or at longer intervals. There are four official products of liver official in the U.S.P. The Liver Extract is a dry, brownish powder orally administered in an average dose of one U.S.P. unit daily. Liver Solution is a brownish liquid to which flavor may be added. It is orally administered in the same average daily dose. Liver Injection is prepared for parenteral use and is administered intramuscularly in the same average dose. Liver With Stomach is a brownish powder made from a mixture of concentrated water solution of mammalian liver and minced fresh hog stomach tissue. It is administered orally in an average daily dose of 1 U.S.P. unit.

This latter product is not strictly a mixture. The liver extract and stomach tissue potentiate each other to produce an effect equal to that produced by larger quantities of either alone. This is probably due to the presence of the intrinsic and extrinsic factors in the stomach tissue.

Liver and kidney are the only organs containing reasonable amounts of the antipernicious anemia principle. The intrinsic and extrinsic factors are responsible for the effect produced by products such as dried stomach and desiccated duodenum. Gastric juice contains the intrinsic factor but no antipernicious anemia principle. Brain and pancreas have some value in anemia but like kidney are not so effective as liver.

There are varying opinions as to the dosage of liver extract. Most authorities agree, however, that parenteral administration (intramuscularly) is preferable in most cases because of its greater effectiveness in reaching a reticulocyte peak. In many cases patients are averse to oral medication and do not take the medicament

as directed or nausea and vomiting may be incurred where the patient cannot tolerate oral liver extract. Presence of severe diarrhea may interfere with absorption of the active principle from the gastro-intestinal tract. Some cases may be particularly resistant and show no improvement when the drug is orally administered. If fever and infection accompany the condition the requirement of drug is too great for oral dosage. Parenteral administration of liver extract is less costly to the patient as well. A concentrated preparation containing 10 to 15 units per cc. is desirable. The frequency of injections depends upon the patient and the severity of the condition. In most cases an injection is given every 2 weeks and in more mild cases once a month. When the case warrants it an injection may be given every week. It is important that the treatment be instituted in a systematic fashion in order to avoid relapses.[7] It is possible in many cases to administer a large dose of the antipernicious anemia product in one injection since the liver is capable of storing large quantities of the active principle.

Massive doses of liver extract are advocated during the first two months of treatment so as to correct the deficiency of the antipernicious anemia principle which exists in the tissues. Following this theory 15 U.S.P. units of liver extract are given each day for 3 days and then once weekly. When the erythrocyte count reaches 4,500,000 to 5,000,000 per cu. mm. the dose is reduced to a maintenance level of 15 units every 4 weeks. This status is usually attained in approximately 7 weeks. The blood should be examined monthly after the third month of therapy and every 3 to 6 months after that. Therapy must be continued throughout the life of the patient.[9]

Clinical improvement in the patient should be noted in 4 to 5 days after therapy is begun. The patient should soon begin to gain weight and notice an improvement in appetite and well-being. Gastro-intestinal symptoms should gradually diminish and the soreness of the tongue disappear. The neurologic disturbances will require more time to diminish. Examination of the blood will show a decrease in the size of the blood cells; the volume index returns to normal and remains so during a course of adequate treatment. Observation of any tendency of the red blood cells to again grow larger is an indication that treatment should be intensified. Another recommended schedule of treatment is 1 cc. of a liver extract containing 15 units per cc. each day for 2 weeks followed by 1 cc. twice a week for 3 months. After this period 1 cc. should be administered weekly for 3 months and then 1 cc. monthly for the duration of the patient's life.[12]

In those cases where the anemia is accompanied by moderate or marked evidences of degeneration of portions of the spinal cord the therapy must be intensified and carried on for a longer period of time. In such cases 200 units of liver extract intramuscularly are advocated for the first week followed by 50 units weekly until the red cell count has increased to 4,500,000 per cu. mm. The dose should then be reduced to 30 units weekly or every 2 weeks until the neurological disturbances have subsided. Following this a maintenance dose of 2 to 3 units daily is necessary. During the first 2 or 3 months 10 mg. of thiamine hydrochloride should be given three times a week.[9]

The dosage of antipernicious anemia principle must be intensified in cases where there are neurological disturbances. In these instances, 20 to 30 units are administered each day for 2 weeks which is then reduced to 3 times a week for 4 to 6 weeks, followed by administration twice weekly for 4 to 6 weeks. Until the neurologic symptoms disappear or no further improvement is possible an injection should be given once a week. This usually continues for about 2 years. Once the neurologic symptoms disappear as evidenced by the return of normal sensation to those upper regions which are involved and a gradual improvement downward from there, the patient may be placed upon a maintenance dose which should be larger than the usual maintenance dose.[13]

In those cases where there are no neurological complications the recommended

dosage is 15 units three times weekly for 2 weeks, reduced to twice weekly for 2 weeks and finally once weekly for a month. If the blood has been restored to normal by the end of this regimen as it should be maintenance doses of 15 to 30 units of liver extract should be administered weekly, monthly or every 6 weeks. This varies with the patient. The time elapsing between each injection should gradually be lengthened by a week every 2 or 3 months. Periodic examination of the blood every 2 or 3 months should be done. Complications such as infections and pregnancy may necessitate an increase in the maintenance dose.[13]

The oral dosage of liver preparations varies with the individual preparation since the strength of each product may vary to some extent. The minimum dose which is recommended is 1 unit daily. This will cause a standard reticulocyte response in the pernicious anemia case which is not accompanied by complications. Many individuals will require dosages in excess of this minimum. The dosage should be sufficient to maintain the blood at a high level of normality. In order to maintain this level and to alleviate the neurological symptoms sufficient liver extract must be given over a period of time. The proper dosage should be determined on the basis of the status of the number of red cells and the hemoglobin content.

Vitamin B

Although the vitamin B complex does not directly influence the status of pernicious anemia it does bear value as an adjunct in therapy. Since anorexia is a factor in this condition thiamine hydrochloride is a valuable stimulant. It also possesses possible value in the relief of the neurological involvements. Patients with pernicious anemia have been shown to be deficient in the vitamin B complex.

Iron

Inorganic iron given orally is of more value in anemia than iron administered parenterally.[14] There is some controversy as to whether ferrous or ferric iron is more effective. It is generally believed that a higher dose of ferric iron is necessary to produce a comparable response to that produced by ferrous iron.

In pernicious anemia iron therapy is indicated in those cases where a deficiency of this element may occur. This frequently takes place in 3 or 4 weeks' time after liver therapy has been instituted. A color index which becomes lower and the hemoglobin rise showing an increasing slowness indicate the need for iron.[13] Some authorities[12, 15] do not believe iron is necessary whereas others consider it of value where the condition is accompanied by malnutrition or chronic hemorrhage.[9]

Hydrochloric Acid

Unless there are gastric disturbances accompanying the achlorhydria in pernicious anemia dilute hydrochloric acid is of little value. In many cases the gastro-intestinal complaints are relieved shortly after antianemia therapy is instituted.[13, 16]

If such symptoms persist relief from the abdominal disturbance and possible control of the diarrhea may be obtained by administration of diluted hydrochloric acid U.S.P. in doses of 10 to 90 minims in half a glass of water. This should be sipped during the meal or afterward.

Another recommendation is the administration of 2 to 4 cc. of dilute hydrochloric acid in a full glass of water, fruit juice or vegetable juice with large meals and sipped throughout the meal. A suitable substitute for hydrochloric acid is glutamic acid hydrochloride which upon contact with water releases hydrochloric acid. Three to 6 capsules of 0.5 Gm. each should be prescribed. One half of the capsules should be taken before and one half after the meal.[9]

Sensitivity to Liver Extract

Sensitivity to liver extract has been noted in an increasing number of cases estimated at approximately 10 per cent of the cases.[7] It is thought that this might be caused by an allergy to pork from which most liver extracts are made.

The reactions incurred have been variable. In some cases a mild local reaction

was noted at the site of injection. In others the symptoms were more severe and included vomiting, urticaria, failure of vision and asthmatic attacks.[16] In a few cases a severe state of anaphylaxis occurred.[7] Oral administration of ephedrine is effective in the milder cases and injection of 0.5 cc. of 1:1000 epinephrine hydrochloride solution controlled the more severe cases. Whenever liver extract is injected a hypodermic of epinephrine hydrochloride solution should be available in case of a reaction. This is more apt to happen in cases where the time lapse between injections has been longer than usual.[9]

If the allergic reaction occurs the brand of extract should be changed. If the patient is found to be sensitive to all brands he must then be desensitized to the extract. This is done by giving 0.1 unit and gradually increasing the dose over a period of 2 weeks. Following the desensitization period the therapeutic doses should be given preferably every 2 weeks and no longer than every 3 weeks.[16]

In patients where there is a history of allergy a skin test might be done in the very beginning and where a strong reaction is noted epinephrine should be injected with the liver extract.

Powdered stomach extract may be given in place of the liver extract in cases of allergy or oral therapy may replace parenteral therapy. The disadvantages of this latter solution are obvious.

Folic Acid

In recent years attention has been directed to the newest member of the vitamin family, folic acid (*L. casei* factor), and its value in the treatment of addisonian pernicious anemia, nutritional macrocytic anemia, sprue and the macrocytic anemias of pregnancy and pellagra.

The synthesis of a single chemical compound found to be effective in treating the above anemias was a milestone in medicine. Late in 1945 the effective use of this compound in the treatment of macrocytic anemia was announced.[17]

Spies[18] recommends five principles to be followed in managing anemia cases. The first principle is to make a correct diagnosis as early as possible in the course of the disease. It is necessary to thoroughly study the patient and the condition of his blood. Persistent and intensive therapy should be started promptly. If folic acid is administered promptly, efficiently and in adequate dosage to the patient requiring it recovery will be surprising. Thirdly, the amount of folic acid given should exceed the amount required to maintain the patient's blood at the normal level. Fourthly, the patient should be instructed to eat foods rich in animal proteins. Throughout the period of convalescence and for the remainder of his life he should be watchful of his diet. In cases where gait and locomotion are disturbed physiotherapy should be instituted. Finally any complicating factors or other diseases accompanying the condition should be treated and eliminated if possible. Unnecessary fatigue should be avoided during convalescence so as to avoid any strain on the heart particularly in older patients.

Folic acid is administered in various dosages dependent upon the individual response. Some patients have been found to respond to daily oral doses of 3 mg. or parenteral doses of 1 mg. whereas others required as high as 10 or 20 mg. Spies[18] states that the ideal dosage has not been determined but from clinical experience he suggests 20 mg. daily either orally or by injection. Apparently folic acid is not harmful in large amounts since as high as 400 mg. have been given daily for a period of three months with no visible bad effects.

Folic acid for injection may be prepared by dissolving it in sterile isotonic sodium chloride solution with a small quantity of sodium bicarbonate to render the solution alkaline. In some cases it may be made by dissolving 1 Gm. of folic acid and 1 Gm. of sodium bicarbonate in distilled water to make 100 cc. of solution. This is sterilized by autoclaving for 30 minutes under 15 lb. pressure.[18]

Patients respond to folic acid in a similar manner as the response to liver extract therapy. The blood is not regenerated any more rapidly and possibly a little more slowly. The same height of blood level

is attained. Tests of the route of administration have shown that response to folic acid is noted when administered orally, subcutaneously, intravenously or intramuscularly and even when given by enema.

Spies[18] has noted in his studies that adequate dosage of folic acid regardless of route of administration elicited a response from all patients with pernicious anemia, sprue and the macrocytic anemias of pregnancy or pellagra. However, many patients with macrocytic anemia associated with leukemia, aplasia of the bone marrow and other conditions showed no response to folic acid, orally or parenterally. A variation in the route of administration in the same patient when response was noted did not alter the response. Liver extract has not shown any effect in cases which did not respond to 20 mg. doses of folic acid.

In those cases where there is a concomitant iron deficiency it is necessary to administer iron as well.

Folic acid has been shown to maintain for at least a year the increased red blood cell and hemoglobin levels caused by liver extract or folic acid. However, folic acid does not always prevent the occurrence of combined system disease nor does it reverse the degenerative process once it has begun. Spies[18] states that, "these observations suggest that until more is known of the mode of action of folic acid in hemopoiesis and until a factor essential to the preservation of the central and peripheral nervous systems is found, liver extract is the safest and most effective therapeutic agent for the routine treatment of pernicious anemia."

Folic acid or pteroylglutamic acid is believed to be a part of an enzyme system. It is found in many foods where it occurs in the form of conjugates. It is believed to be stored in the tissues as an inactive conjugate. The enzymes necessary for splitting off the folic acid are thought to be lacking in pernicious anemia. Patients with nutritional macrocytic anemia, pellagra and sprue have been observed to be capable of utilizing the conjugates.

The fact that large amounts of folic acid are necessary in comparison to relatively small amounts of liver extract led to the theory that the folic acid conjugates may be stored in the body until a substance which affects the cellular constituents of bone marrow is liberated by a factor in the liver extract.

It is important to remember in all of these cases of pernicious anemia that no set regimen can be followed for every patient for each case has its own peculiarities which must be considered in deciding upon the necessary dosage. It is most important that sufficient dosage be given regularly and the dosage increased when indicated since the individual requirements may vary at different times. In resistant cases other complications such as infection, degenerative developments, or renal disease should be considered.

Bed rest is not absolutely necessary in pernicious anemia unless there are complications. The patient may be as active as is permitted by his condition

The diet is important in the control of pernicious anemia. Animal protein preferably in the form of pork or beef should be included in adequate quantities. Since the meat should not be too thoroughly cooked it may be necessary to use beef almost entirely and occasionally use well-cooked pork rather than run the risk of the trichinosis in pork which is not well-cooked. The diet should also contain adequate amounts of all of the vitamins and in severe cases should be supplemented by balanced therapeutic doses of the vitamins.

Many of the usual products used as adjuncts in anemia therapy such as the combinations of iron, liver and vitamins now include folic acid.

Sprue

Sprue is a disease with which a macrocytic anemia is associated. It is chronic and is believed to be caused by a dietary deficiency. It occurs mainly in the tropics and subtropics. Examination of the blood reveals the presence of large erythrocytes and a high color index comparable to that of pernicious anemia. The leukocyte count is lower in number than normal and relative lymphocytosis exists. In sprue the bilirubin content of the blood is not so steadily increased as it is in pernicious ane-

mia.

The symptoms of sprue, which usually is insidious in onset but may be sudden, include an abundant foamy diarrhea, cachexia, loss of weight, neurological disturbances in some cases, and sore tongue. The abdomen often protrudes. More common in sprue than in pernicious anemia is the sore tongue and the loss of weight and cachexia are usually more severe than in pernicious anemia. Achlorhydria may be present also. This condition may be differentiated from pernicious anemia by an examination of the stool and a study of the patient's history. The anemia in sprue is thought to be due largely to insufficient absorption of the antipernicious-anemia principle from the small intestine as a result of the diarrhea. A diminished ingestion of the extrinsic factor is also partly responsible.

Dietary treatment may be all that is necessary to relieve this condition. If this is insufficient liver extract in doses similar to those for pernicious anemia should be given. As the condition improves the liver may be given orally, but this change should be made cautiously. As in pernicious anemia the dose of liver extract must be changed as the condition improves.

Nicotinic acid is of value and is present as a factor in the more crude liver extracts. Therapy with folic acid has been described above.

Large quantities of protein, milk, fruit and leafy vegetables should be included in the diet.

Frequently the anemia associated with sprue is normocytic.

Pellegra

A study of the blood picture in patients with pellegra reveals the presence of an anemia which may be macrocytic, normocytic or hypochromic. Pellegra is caused by a deficiency of nicotinic acid, a factor in the vitamin B complex. Chronic alcoholism is sometimes responsible not as a direct cause but due to the fact that in most cases alcoholic beverages are substituted for food. Consequently the individual does not receive the necessary elements for his well being. It also occurs more frequently in warm climates. Dermatitis, dementia and diarrhea are the most outstanding symptoms. The patient frequently suffers from headache, insomnia, depression and dizziness. The dermatitis is intensified on exposure to sun. The tongue becomes exfoliated or ulcerated or develops an atrophic glossitis as shown by a smooth, red surface. Excessive salivation may occur and the salivary glands may protrude. Diarrhea is usually present particularly when achylia gastrica occurs.

The anemia is probably caused by insufficient intake of the extrinsic factor. The history of deficient diet, dementia, diarrhea and the dermatitis all serve as a diagnostic aid in differentiating pellagra from pernicious anemia.

Specific therapy for pellegra is nicotinic acid or nicotinamide. It is necessary to treat for the deficiency rather than for the anemia. Liver extracts have shown some effect but this is believed to be due to the presence of nicotinic acid in the extract. Crude extracts contain more nicotinic acid than the more refined products. The use of folic acid has been described previously.

Pernicious Anemia of Pregnancy

A macrocytic anemia is sometimes associated with pregnancy. The blood picture is the same as for pernicious anemia and it is caused by the same factors which are responsible for pernicious anemia although it is believed that an added impetus is given it by the demands of the fetus for hemopoietic substance. The most common anemias of pregnancy are normocytic or hypochromic microcytic which will be discussed later.

The chief cause of this anemia is a decreased supply of the intrinsic factor which results from suppression of gastric acidity. Also partially responsible is a deficiency in the ingestion of the extrinsic factor. This too can be traced to the demands of the fetus as well as an uncertain appetite. Neurological disturbances rarely occur. Examination of the gastric juice may or may not show free hydrochloric acid present.

Some have called this puerperal anemia since it has been discovered in the puer-

perium. Usually the anemia is observed in the third trimester. It may develop gradually or suddenly. When specific therapy is stopped following delivery no relapse occurs as it does in true pernicious anema when therapy is stopped.

Liver extract therapy is indicated in this type of anemia. The schedule of doses for addisonian pernicious anemia are effective but better results are obtained with larger doses. The use of folic acid has been described previously.

There are several less common conditions with which a macrocytic anemia may be associated or which may cause it. These will be discussed briefly.

Infestation with Fish Tapeworm

Examination of the stool for ova of the fish tapeworm should be done in cases of macrocytic anemia particularly if the patient is an Indian, a Finn or from the Great Lakes Region of the U. S. Such an anemia may result from ingestion of raw or only partially cooked fish. A soluble toxin is probably formed which in turn is a factor in the development of an anemia.

In such cases it is of course of first importance to rid the patient of the parasite. However, liver extract will improve the blood picture in the interim. The dosage is usually 10 U.S.P. Units daily for 3 days and then 10 units twice a week until improvement is noted.

Gastrectomy Anemia

Patients who have had gastrectomies sometimes develop a macrocytic anemia due to a deficiency of both the intrinsic and extrinsic factors. The dosages in this condition are the same as for addisonian pernicious anemia.

Chronic Obstruction of the Small Intestine and Cirrhosis of the Liver

Macrocytic anemia sometimes is observed in patients with a chronic obstruction of the small intestine. It is thought to be due to a lack of the extrinsic factor and a deficiency in the absorption of the antipernicious anemia principle as a result of vomiting and diarrhea.

Cirrhosis of the liver is caused by various agents. The macrocytic anemia associated with this condition is probably caused by the interference with the liver's function of supplying the hematopoietic principle to the bone marrow. It is possible also that the intestinal absorption of the antipernicious anemia principle may be affected.

Liver extract is administered intramuscularly to these cases in the same dosage as for addisonian pernicious anemia. Adequate vitamin therapy, particularly of A, B_1, B_2 and the complex, is also necessary.

The cirrhotic condition of the liver is of course subjected to the proper therapy. Such therapy may consist of the daily oral administration of 2 Gm. each of methionine and choline chloride accompanied by daily parenteral administration of aqueous whole liver extract with vitamin B complex supplement. In such cases the diet is also important. It should contain the maximum amounts of protein-carbohydrate and the minimum quantity of fat accompanied by casein supplements.[19a]

Goat's Milk Anemia

A rare disease in the United States is the macrocytic anemia caused by a deficiency in the extrinsic factor and probably a deficiency in mineral content of goat's milk when used for infants on an exclusive milk diet. Liver and stomach extracts along with iron and vitamin B complex are recommended.

Erythroblastosis fetalis

The blood picture in erythroblastosis fetalis shows a greatly reduced erythrocyte count but usually an increase in the number of leukocytes. The total hemoglobin is low but high in the individual cells. The platelet count may be reduced. The white cells show leukocytosis, myelocytes and occasionally myeloblasts. During recovery eosinophilia is observed. The red blood cells show erythrocytosis of the macrocytic type, reticulocytosis, stippling, large numbers of erythroblasts and megaloblasts, and polychromatophilia. The fragility of the cells is usually normal. Hemorrhagic diathesis may be present and the bleeding time may be longer than nor-

mal. The urine shows evidence of bile. The icterus index is increased and a positive van den Bergh reaction, frequently biphasic, is observed.

This condition rarely occurs in the first newborn child. It is the result of an Rh factor incompatibility. As noted from the blood picture the anemia is severe and is macrocytic and hemolytic. The baby shows lethargy and lassitude and may develop hemorrhages and convulsions. Petechial hemorrhages may take place. The liver and spleen are enlarged and a mahogany-brown jaundice is observed. If the infant is able to survive the jaundice he will recover spontaneously in a period of approximately 4 months. In mild cases the condition is self-limiting. Mental deficiency and spastic diplegia may result if there is a residual cerebral damage caused by injury to the basal ganglia. Liver therapy is of very little value in these cases.[5,6,20]

Prompt transfusion seems to be the only therapy of value. The blood employed should be Rh negative and should be obtained from donors with the same blood group as the mother, the infant or from group O donors. Anti-A and anti-B agglutinins in the serum should be weak if possible. Neither of the parents' blood should be used. The quantity used is 10 to 15 cc. per pound of body weight every 24 hours or as often as is necessary to maintain the red cell count above 2,000,000. If Rh negative blood is not available Rh positive blood cells should be removed from the plasma and suspended in normal saline. This eliminates the agglutinins. Rh negative blood is preferred since the Rh positive donor cells may be hemolyzed in a few days by the Rh positive agglutinins inherited from the mother and present in the fetal blood. Rh negative donor cells remain available for approximately 90 days.[16,20]

Severe erythroblastosis may be treated by simultaneous removal and replacement of the blood of the newborn infant. This method has been successful in some cases. In order to prevent shock due to exsanguination the Rh positive blood is withdrawn from the sagittal sinus simultaneously with the administration of Rh negative blood through a cannulated vein. If this procedure is continued for 60 minutes, if the mixing is considered to have taken place at the right rate, and if the baby's blood volume is approximately 250 cc., only 36.7 per cent of the original blood remains. This percentage may be reduced to 25 per cent by varying the procedure. Fifty cc. of blood are removed and then 50 cc. administered in alternation.[20a]

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—To be continued

CANCER

Serial Surveys of Current Concepts and Activities

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Carcinoma of the Lung

In 1944 there were 71,590 deaths from all causes in New York State, exclusive of Metropolitan New York.* Of these 9,388 were from "Cancer and Other Malignant Tumors" (13.1 per cent). Of the deaths from cancer and other malignant tumors 419 (4.4 per cent) were from cancer of the lung.

There is at present no separation, so far as this department has knowledge, into the number of primary lung cancers and metastatic lung cancers.

THE PRESENT STATUS OF THE SURGICAL TREATMENT OF PRIMARY CARCINOMA OF THE LUNG. WILLIAM FRANCIS RIENHOFF, JR. JOUR. AMER. MED. ASSN., 126:1123 (DECEMBER 30) 1944.

The first total pneumonectomy, performed in the Johns Hopkins Hospital for primary sarcoma, was done July 24, 1933. The patient, a girl aged 3½ years, made a "remarkably uneventful recovery." She died an accidental death when she was 8 years of age. An autopsy "showed no recurrence of the original growth, nor any abnormality of the remaining thoracic viscera, except a compensatory dilation of the right lung."

Since then there have been 181 consecutive cases of primary lung cancer treated with pneumonectomy. These cases are analyzed in this study.

OPERABILITY: 71 (39.2 per cent) of the patients were operable and 110 were inoperable "at the time of exploration" (patients seen and found inoperable are not included in the study).

INCIDENCE: Primary pulmonary cancer is increasing. The author takes a conservative view of the reason by this statement: "In the series of cases reported (in the literature) the majority of authors agree that the constant inhalation of irritating substances undoubtedly plays an important part."

SIGNS AND SYMPTOMS: COUGH (in 71.0 per cent of the cases.) "In a nation of heavy cigarette smokers, in which the population . . . breathes the polluted atmosphere of cities, cough is almost universal and is due to nonspecific irritation of the respiratory tract." "If in an 'adult chronic cougher' the type of cough changes to a spasmodic, productive or nocturnal type . . . attention should be focused on the bronchial tree and the presence of a bronchial neoplasm should be suspected."

HEMOPTYSIS (in 63.0 per cent). "Unless the x-ray and sputum examinations are indisputably those of tuberculosis or bronchiectasis, hemoptysis must be considered to be due to an intrabronchial growth until it has been ruled out by the many types of examination at our command."

PAIN (50.0 per cent). LOSS OF WEIGHT (39.0 per cent). HYPERPNEA (23.0 per cent).

PNEUMONITIS (18.0 per cent). FEVER (13.0 per cent). TIGHTNESS IN THE CHEST (3.0 per cent).

ROENTGENOGRAMS were positive in every instance. Whenever "roentgeno-

* Sixty-fifth Annual Report of the Department of Health of the State of New York. (2:35, Table 14).

grams of the chest show a departure from the normal and in which this departure is not in every way characteristic of one of the commoner lesions of the lungs, the presence of bronchogenic carcinoma should be inferred."

An infiltrating hilar shadow in a patient past middle age, associated with cough, hemoptysis, and the absence of tuberle bacilli in the sputum almost certainly indicates a bronchogenic carcinoma. In the author's experience BRONCHOSCOPY, next to roentgenography, is important in diagnostic procedure. It allows for direct vision and BIOPSY. BRONCHOGRAPHY is less important and ASPIRATION BIOPSY is condemned.

"Exploratory thoracotomy should be resorted to far more frequently in the future that it has been in the past . . . The impression that all primary malignant tumors of the lung are slow growing and are late in metastasizing is incorrect."

HISTOLOGICALLY, 50.0 per cent of growths in these 181 cases were squamous cell carcinomata and 14.0 per cent were flat cell carcinomata; 28.0 per cent adenocarcinomata; 40.0 per cent cylindrical cell growths; and 4.0 per cent oat cell tumors.

Total pneumonectomy was done in seventy-one (39.1 per cent). In 70.0 per cent of these, metastasis to the bronchial and tracheal lymphnodes was found.

With one exception, of the patients who survived to be discharged from the hospital, those with the flat cell type of tumor lived longer than those with the adenocarcinoma type. Twenty of the former type lived from seven months to two years and ten months; eleven of the adenocarcinoma type lived from three months to three years and three months. Nineteen of the patients are still living at the time of writing the report. The longest period since operation was eleven years. There were six five-year survivals.

The author concludes his paper as follows: "An otherwise fatal disease, primary carcinoma of the lung can be satisfactorily treated with surgical removal of the entire organ. Surgical measures short of total pneumonectomy are not efficacious. Postoperative mortality and longevity are at least as good as, if not better than, the postoperative results following the surgical treatment of other organs."

This paper by Rienhoff, Jr., covers the treatment outlook from 1933 to 1944. This year (1947) an analysis of 343 cases of primary bronchogenic carcinoma brings us the present problem, which is to look with suspicion on the patient in the older decades who has a winter cough, accompanied by afternoon fever and loss of weight, perhaps also by pleural effusion. Perhaps this patient has a primary bronchogenic cancer.

BRONCHIOGENIC CARCINOMA; AN ANALYSIS OF 343 CASES. R. K. HOLLINGSWORTH. ANN. INT. MED., 26:377 (MARCH) 1947.

There are two periods of delay during which a patient with symptoms pointing to the possibility of pulmonary cancer may forfeit his chance for cure; "the first is between the onset of symptoms and medical consultation, and the second is that between the first medical consultation and a positive diagnosis."

With these facts in mind the author has made a survey of 343 cases seen in the various services at the University of Michigan Hospital (Ann Arbor) during the six years from January 1, 1938, to January 1, 1944. The cases are divided into two groups: 112 in which histologic confirmation is lacking, although clinically and roentgenologically the diagnosis was justified; and 231 in which the diagnosis was confirmed by histological study.

The most frequent initial symptoms are cough leading to a diagnosis of pneumonia, "flu" and "cold"; they were present in 160 of the patients or 69.2 per cent of those in which histologic studies were possible.

There were two main clinical types of growth; peripheral and hilar. Histologically, the neoplasms were recorded as squamous cell (98), adenocarcinoma (the gland cell type) (45), and undifferentiated cell type (81). In seven cases the cell type was not determined.

In more than one-half the cases a diagnosis of bronchogenic carcinoma was not made until six or more months had passed after the patient sought medical advice.

Roentgen-ray study of the chest, bronchoscopy and biopsy studies and bronchography, which "is useful at times," should be used as aids to diagnosis.

In the 231 cases only seventy-seven were considered operable (33.3 per cent), and of these in only forty-three was resection possible. Seventeen (39.5 per cent) of the forty-three cases survived operation for from two months to seven years.

"Bronchogenic carcinoma is a relatively slowly growing" and slowly metastasizing neoplasm; for this reason early diagnosis is essential for statistical improvement in successful treatment figures.

In order to be quite accurate the suspicion should always be borne in mind that a pulmonary cancer is metastatic, even when the lung involvement is in the form of a single lesion. Often the primary growth is in the intestine somewhere.

MILIARY CARCINOSIS OF THE LUNGS SECONDARY TO PRIMARY CANCER OF THE GASTRO-INTESTINAL TRACT. GORDON J. CULVER. AMER. JOUR. ROENTGENOL., 54:474 (NOVEMBER) 1945.

A report of four cases in which miliary carcinomatous nodules were found in the lungs.

The route by which carcinomatous emboli may travel from an intestinal tumor to the lungs is suggested as (1) to the regional lymphnodes, (2) to the thoracic duct, (3) to the junction of the left subclavian and left internal jugular veins to (4) the right heart and (5) through the pulmonary artery to the lungs.

An alternative route would be from the intestinal tumor (1) to the liver through the portal system (2) to the inferior vena cava to the right heart (3) to the lungs.

Differential diagnosis between miliary carcinosis and miliary tuberculosis and silicosis is to be considered. In miliary tuberculosis the lesions are usually more discrete and of more uniform size and the individual nodules have a more homogeneous density.

In silicosis the mid lung fields exhibit the greatest degree of involvement. The nodules appear hard and of quite uniform size. There is usually an associated peribronchial fibrosis and large, dense, hilar shadows.

The lack of positive physical findings is a characteristic clinical feature in carcinosis. The absence of physical signs in the chest would tend more toward than against a diagnosis of miliary carcinosis in the presence of suggestive roentgen findings.

Two of the cases showed primary cancer of the gallbladder with secondary invasion of the liver both by direct extension and by circulatory spread.

One case showed carcinoma of the pancreas with secondary lymphatic spread to the supraclavicular nodes.

One case showed thoracic duct spread from a carcinoma of the stomach although there was no confirmation by necropsy.

ADENOMA OF THE BRONCHUS. HERMAN J. MOERSCH, WILLIAM S. TINNEY AND JOHN R. MCDONALD. SURG. GYN. OBSTET., 81:551 (NOVEMBER) 1945.

A study of thirty-eight consecutive cases of adenoma of the bronchus from the Divisions of Medicine and Pathology in the Mayo Clinic (Rochester, Minnesota).

The authors conclude that the tumor is a slow growing growth that gives rise to clinical symptoms over a much longer period than carcinoma does. Cough is the earliest and most frequent symptom. Other symptoms are: hemoptysis, asthmatoid wheeze and recurrent attacks of pulmonary infection. The cell type is small, round, without mitoses and without hyperchromatism of the nucleus. The cells "consistently make an attempt to form acini but are rarely very successful."

There were no metastases and there were no instances of bilateral tumors.

Endoscopic destruction of the tumor or lobectomy are the methods of choice in the treatment. In this series there were nine cases treated with Pneumonectomy;

—Concluded on page 313

MISCELLANY

The General Practitioner In the Hospital

The following matter is a recent report of the Council on Medical Education and Hospitals to the House of Delegates of the American Medical Association:

Considerable thought has been given to devise ways of upholding the prestige of general practitioners so that they may be encouraged to provide the citizens of our country with the kind of medical care which they are peculiarly qualified to furnish and for which there promises to be continued need.

The establishment of a Section on the General Practice of Medicine by this House in 1945 was an important step forward. Interest in this section was at once apparent as shown by a registration of 939 at the 1946 Scientific Assembly and by the attendance of these registrants at the various meetings. This House has also expressed its approval of the organization of sections on general practice in state and county medical societies.

In spite of this, certain hospitals have inaugurated as a matter of policy limitation of their staff appointments to physicians certified by specialty boards or holding membership in certain special medical societies. Such a policy is contrary to the principles of the Council and seems unsound. In publications which have dealt with hospital standards, the Council has expressed repeatedly the need for a hospital staff of high quality; it has never mentioned certification by a specialty board or membership in a special medical society as an important credential.

Certain institutions have assured for themselves the inclusion on their staffs of properly qualified general practitioners by the intra-mural establishment of "General Practice Sections." An excellent description of how such a section actually operated over a period of eight years in a 450-bed hospital appeared on pages 15 through 16 of the May 3, 1947 issue of The Journal. Reprints of this article will be distributed by the Council to every registered hospital in the United States.

On the whole, so much uncertainty appeared to exist in the minds of many boards of trustees of hospitals about the propriety of establishing such sections as to lead this House at its meeting in San Francisco a year ago to adopt a significant resolution. This was reported favorably by the Reference Committee on Medical Education and adopted by the House; part of this resolution is quoted:

"WHEREAS, Many hospitals have not established general practice sections in their visiting active staffs and their governing heads are doubtful whether such action has the approval of the bodies which set up the rules and regulations for the approval of their hospitals for interns and residents; therefore be it

Resolved, That hospitals should be encouraged to establish general practitioner services. Appointments to a general practice section shall be made by the hospital authorities on the merits and training of the physician. Such a general practice section shall not per se prevent approval of a hospital for the training of interns and for residencies. The criterion of whether a physician may be a member of a hospital staff should not be dependent on certification by the various specialty boards or membership in special societies."

Copies of this resolution have been sent to the American College of Surgeons, the American College of Physicians, the Amer-

ican Hospital Association, the Protestant Hospital Association, the Catholic Hospital Association and to each hospital registered by the Council.

To further carry forward the intent of the resolution, the following report was published by the Council in The Journal, page 95, in the May 3, 1947, issue:

"At the direction of the House of Delegates of the American Medical Association some years ago, the Council on Medical Education and Hospitals formulated standards for the establishment of American boards for the certification of specialists and for the conduct of hospital residencies providing training in the various special fields of medicine. The aim was to improve the quality of training at this level of medical education. The physician responsible for directing such hospital training should himself have had training and experience approximately equivalent to that required of certification applicants, whether or not he is actually certified. But it was never intended that staff appointments in hospitals generally, or even in hospitals approved for residencies, should be limited to board certified physicians, as is now the policy in some hospitals. Such policies, if practiced extensively, are detrimental to the health of the people and, therefore, to American medicine. Hospital staff apointments should depend on the qualifications of physicians to render proper care to hospitalized patients, as judged by the professional staff of the hospital, and not on certification or special society memberships.

"In this opinion the Council has the full concurrence of the Advisory Board for Medical Specialties, which represents all of the American Boards in the specialties. At the February 1947 meetings of the Advisory Board it was unanimously voted to adopt as the sentiment and policy of the advisory Board the recent resolution passed by the American Board of Surgery, which reads:

'The American Board of Surgery is not concerned with measures that might gain special privileges or recognition for its certificants in the practice of surgery. It is neither the intent nor has it been the purpose of the Board of Surgery to define requirements for membership on the staffs of hospitals. The prime object of the Board is to pass judgment on the education and training of broadly competent and responsible surgeons—not who shall or shall not perform surgical operations. The Board specifically disclaims interest in or recognition of differential emoluments that may be based on certification.'

"Since February, several separate American Boards in the various specialties have taken similar action. The Council on Medical Education and Hospitals of the American Medical Association is completely in accord with this principle."

The Council now asks authority to use still another lever to carry forward the intent of the resolution. It recommends that Section 3, paragraph 6, of the "Essentials of a Registered Hospital" now reading:

"6. Staff sections, such as medicine, obstetrics and surgery, should be organized as may seem wise"

to be amended to read:

"6. Staff sections, such as medicine, obstetrics, surgery, general practice, etc., should be organized as may seem wise."

This amendment is proposed in the belief that even so small a change in wording of the Essentials may be of help in promoting the intent of the resolution adopted by this House a year ago.

The desirability of doing this is plain. The establishment of an American Board of General Practice is being discussed by the Section on the General Practice of Medicine, by the Council and by the Advisory Board for Medical Specialties. The wisdom of establishing such a specialty board at this particular time is debatable. Wider realization and greater use of the contributions which skillful general practitioners can bring to hospitals may make superfluous the need for their certification by a specialty board.

CONTEMPORARY PROGRESS

MEDICINE

Results of Treatment of Pneumococcic Lobar Pneumonia and Other Acute Infections with Several Oral Penicillin Preparations

W. S. Hoffman and I. F. Volini (*American Journal of Medical Sciences,* 213:520, May 1947) report the use of oral penicillin in the treatment of pneumococcic pneumonia and other infections due to penicillin-sensitive organisms. In previous assays of the penicillin preparations used, it had been found that an initial dose of 200,000 units followed by 100,000 units every three hours gave therapeutically effective blood plasma concentrations of penicillin similar to those obtained with 20,000 units given intramuscularly every three hours. Oral penicillin on this dosage schedule was employed in 49 patients with pneumococcic lobar pneumonia; 77 per cent of these patients showed subsidence of fever and toxemia within forty-eight hours, in some cases within twelve hours. In the cases in which the treatment failed to bring about prompt improvement, failure was due either to inadequate absorption, as indicated by the plasma penicillin levels, the presence of a penicillin-insensitive organism such as a virus, the presence of penicillin-resistant pneumococci, or to overwhelming complications. There was one death in the series; in this case the pneumonia was bilateral, but pneumococci were not isolated from sputum (by mouse inoculation). The 81 patients with other types of acute infections responded well to oral penicillin, those with hemolytic streptococcic infections rapidly, and those with staphylococcic infections more slowly. The results in these cases were similar to those obtained in infections of the same type with intramuscular penicillin. The plasma penicillin levels in this series of cases were usually 0.06 unit per cc. or more during the three-hour interval between doses, as was indicated by the previous assays of the oral penicillin preparations employed. The various preparations appeared to be equally effective therapeutically except that crude calcium penicillin was less effective than any of the others. Urticaria developed in 3.8 per cent of the 180 cases in this series; but the incidence of urticaria was only 0.86 per cent in a total of 580 subjects given oral penicillin for assays or treatment. When purified preparations were used only 2 spurious cases of urticaria occurred.

COMMENT

Oral penicillin is effective in pneumonia. Perhaps it is well to give the first dose parenterally. Penicillin, of course, is not effective in the virus type of pneumonia.

M.W.T.

A New Drug for the Control of Cough in Chronic Pulmonary Disease

C. Rudner (*Southern Medical Journal,* 40:521, June 1947) reports the use of hycodan bitrartrate (dihydrocodeinone) in the treatment of cough in chronic pulmonary disease, especially in pulmonary tuberculosis. This drug is closely related to codeine chemically, but has proved more effective than codeine in controlling cough in the cases in which it has been employed. Of the first 50 patients given hycodan bitartrate for the relief of cough, 44 had active pulmonary tuberculosis, 2 had healed pulmonary tuberculosis with residual bronchiectasis, 2 had chronic lung abscess and one each primary atypical pneumonia and bronchiogenic carcinoma. The drug was given three times a day immediately after meals and at 9 p.m. with a little milk; with this schedule there were no side reactions. Thirty-three of the tuber-

culous patients and all the non-tuberculous patients had been given codeine for control of cough, with practically no relief in 15 of the tuberculosis cases and 4 of the non-tuberculous cases. All the others reported more satisfactory relief with hycodan. Hycodan relieves cough without entirely suppressing productive cough; it has proved especially useful in the emetic cough of fibroulcerative pulmonary tuberculosis. It has not caused either addiction or tolerance.

COMMENT

Hycodan is a useful drug. I have used it not only for cough but for other conditions for which codeine is prescdibed.

M.W.T.

Infectious Hepatitis: Clinical and Laboratory Features of 295 Cases

H. J. Zimmerman and his associates (*American Journal of Medical Sciences,* 213:395, April 1947) report a study of 295 cases of infectious hepatitis occurring in Army personnel in eastern France between February 15 and June 14, 1945. In two-thirds of this group the symptoms at onset suggested influenza, but in half of these cases the associated anorexia, epigastric distress and dark urine indicated the correct diagnosis; in the other cases in this group several days elapsed before signs of liver involvement developed. Clinical jaundice developed in 90.2 per cent of cases. In most of these cases the icterus index was between 40 and 49. In the small percentage of patients not showing clinical jaundice, the general symptoms were the same as in those with jaundice, but the course of the disease was milder. In the patients with jaundice the severity of the disease and its duration was roughly proportional to the degree of icterus. On admission to the hospital, the liver was palpaby enlarged in two-thirds of the patients; enlargement of the lymph glands, involving the cervical glands alone or generalized, was common. Bradycardia was noted in 40 per cent, and fever was present in 70 per cent. As a rule the abdominal pain, anorexia and headache, present on admission, decreased in severity when jaundice developed, but pain in the epigastrium often persisted for four or five weeks; malaise and anorexia subsided gradually. Itching, which was present in only 20 per cent of the patients on admission, developed at some time during the disease in 70 per cent. Bed rest was enforced during the acute phase of the disease and early convalescence. All patients were given a diet high in protein (2 gm. per kg. body weight daily) and low in fat with a caloric value of 2500 daily; the protein intake was supplemented by feedings between meals of skimmed milk enriched by egg albumin. Plasma was given to patients who could not eat and to others who were severely ill. The criteria of recovery were absence of pain or bloating, absence of tenderness in the epigastrium or right upper quadrant, subsidence of liver enlargement (or at least absence of tenderness over the liver); presence of normal appetite and return of a feeling of well-being; normal sedimenta-

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tion rate; normal icterus index for at least two weeks; and urobilinogen in the morning urine below 2 mg. per 100cc. When these criteria were satisfied, patients were given a ten-day program of physical exercise, and were discharged as cured if no symptoms developed. If symptoms persisted over sixty days, the condition was considered to be subacute, and the patients were discharged to another hospital outside the theater of operations. There were relapses in 23 cases, most of which were due to excessive activity when the patient should have been resting; there was no correlation between the severity of the initial attack and the incidence of relapse. There There were no deaths in this series, although in 6 cases, fever, extreme lethargy, drowsiness, severe nausea and vomiting developed after the jaundice had begun to subside—a clinical syndrome that often precedes death. Illustrative cases are reported.

Myeloblastic Leukemia, Terminal Stage of Panmyelophthisis

A. Leye (*Helvetica Medica Acta,* 14: 174, April 1947) reports that at the University of Basle, since 1933, 104 cases of blood diseases of various types have come to autopsy. Of these 70 were leukemia—myeloid leukemia 25 cases, lymphatic leukemia 23 cases and myeloblastic leukemia 22 cases. There were 10 cases of anemia, 7 of which were pernicious anemia, 16 cases of agranulocytosis, and 8 cases of panmyelophthisis, one of which showed myeloblastic leukemia in the terminal stage. In panmyelophthisis, all the cellular elements of the blood are reduced; there is anemia, granulocytopenia and thrombocytopenia; the bone marrow in true panmyelophthisis is aplastic. Yet in some cases with the clinical symptoms and blood findings of panmyelophthisis, autopsy may show a cellular rather than an aplastic bone marrow. For this reason the clinician should use the term panmyelopathy (Naegeli) or panhemocytophthisis (Glanzmann) to designate such cases. In the case reported in which myeloblastic leukemia was the terminal stage of a "panmyelophthisis," the patient was twice admitted to the hospital, in May 1941 with a diagnosis of agranulocytosis; he was discharged the last of June with a diagnosis of cured panmyelophthisis. He was admitted again in September (1941) with a diagnosis of anemia; there was a history of bleeding from the gums and several attacks of nosebleed in the last three weeks; blood counts showed a myeloblastic leukemia; he died on the eighth day, the white cell count dropping suddenly from 200,000 to 400 on the last day of life. Autopsy showed an aplastic bone marrow with the presence of granulated basophiles, characteristic of severe panmyelophthisis. Myeloblasts were present in various organs in the form of perivascular infiltrations, especially in the liver in the capsule of Glisson, as has been noted in other cases of myeloblastic leukemia. In recent years others have reported cases of true panmyelophthisis and of clinical myelopathy (without aplastic bone marrow), in which acute myeloblastic leukemia developed in the terminal stage. In the case reported and in other cases of acute myeloblastic leukemia, the author has observed a sudden decrease in the white cells—including the myeloblasts—just before death. This also has been noted by others. This same decrease in total white cell count and myeloblasts is also observed in remission in myeloblastic leukemia. These findings indicate that myeloblastic leukemia is due to some fault in the regulation of the production of the myeloid elements and that such disturbances may be associated with panmyelophthisis.

PHYSICAL THERAPY

The Implications of Hydrotherapy

M. B. Ray (*Archives of Physical Medicine,* 27:742, Dec. 1946) discusses various methods of hydrotherapy and their indications. For the optimum effect of an immersion bath a warm pool is required. At the British Red Cross Society's Clinic in London, such a pool is provided in which

the water is kept at a temperature of 100°F. by means of an underwater douche that delivers water under pressure at a temperature 10° higher than that of the water in the pool. The underwater douche can be directed against the submerged parts of the patient's body for which special treatment is required; it has a marked analgesic effect. Provisions for underwater exercises in the pool are also made. Such pool baths are of value in arthritis and in the treatment of poliomyelitis. Hot immersion baths are "an almost universal remedy" for muscle fatigue and stiffness following strain and injury; they may also give symptomatic relief in spasmodic conditions, such as dysmenorrhea, hepatic or renal colic. Hot baths, artificially medicated or naturally mineralized with a saline substance, are of special value in rheumatic affections. Hot peat baths, in which water is mixed with mud or peat to the consistency of thick porridge are also of value in the same conditions; such peat baths retain their heat for a much longer period than water baths. Partial baths, including sitz baths, depend for their efficacy to a great extent on the fact that the local application of heat produces a general reaction—progressive vasodilation, and increased circulation in the capillaries and veins. The sitz bath relieves the congestion of the deeper organs. The glove bath, with the hands encased in rubber gloves, or the foot bath, with the feet encased in rubber socks reaching half way up the calf, immersed in water at a temperature of 110° to 120°F. may be given for twenty minutes to half an hour on alternate days. This is of value in the treatment of arthritis with stiffness, pain, swelling and deformities in the wrists and fingers or ankles and feet; in sprains and strains of ankle or wrists, and stiffness following injuries. Another method of hydrotherapy that is of value is the full wet pack or local wet packs. These may be applied either hot or cold, according to indications. In cases of insomnia, delirium or general restlessness, the full wet pack can induce sleep that is far more refreshing and normal than that induced by hypnotic drugs.

Comment

The author quotes Lowman and others on the superiority of hydriatic measures to ordinary medical gymnasium methods, as exercise and massage. 1. In water there is no fixed resting-place. Muscles contract and/or move both origin and insertion and therefore there is greater freedom of action. 2. In water a flow of fixative effort goes completely around the body as around a cylinder. More "synergists" are called into play by the difficulty in obtaining stability. Consequently, a strong muscle not balanced assumes greater activity—hence greater importance. Even though a muscle has received special intrinsic training for years and has apparently reached its maximum of recovery in air, it may improve still further in underwater work.

The whirlpool bath, giving heat, and the hydromassage from the air bubbles, inducing the patient to exercise of his own volition, is one of our best general measures, in poliomyelitis, arthritis and allied conditions, multiple contusions, fractures, burns, dislocations, muscular fatigue, strain or injury.

Locally, in traumatic lesions as sprains, fractures, dislocations, contusions, spasm or paralysis, early movement under water induces confidence and comfort and soon sets the patient on the road to his job.

The partial bath was described by Professor Georg Hauffe many years ago. He divided local heat stimuli into (1) sudden or sharp, either hot or cold and, (2) slowly rising by heat. Dr. Fortescue Fox immersed both arms in a single bath at "blood heat". Heat is gradually increased about 1°F. per minute, beginning at 100°F. Continuing from 12 to 20 minutes, 120°F. would be the final temperature. In vascular hypertension the fall in blood pressure is from 5 to 15 mm. diastolic, lasting from 2 to 6 hours. Pain and dyspnea are relieved. In chronic conditions (as arthritis or allied affections), with poor circulation, cold, chilling, Raynaud's disease or chilblains, it is of great service.

"Baking and/or massage" and the exercise of spastic muscles, in paralytics, is still being done hourly, daily, weekly, monthly and yearly, by operators not properly supervised, when underwater exercise with its heat and massage would clear up disabilities in a matter of weeks, if seen early, and a matter of a few months where delayed.

Delay in instituting these measures, as soon after injury as possible, is what makes for irreversible lesions and chronic disabilities. These latter call for strenuous methods of rehabilitation that use up a vast amount of energy, time, physical and mental labor, on the part of patients, physicians, nurses, technicians and other personnel, leading to deficits in hospital, family, city, county and federal budgets. ***M.C.L.McG.***

Rehabilitation After Injuries to the Spinal Cord and Cauda Equina

L. Guttmann (*British Journal of Physical Medicine*, 9:130; 162, Sept.-Oct. and Nov.-Dec., 1946) briefly describes the methods of general treatment and psychotherapy employed for patients with injury of the spinal cord and cauda equina at a British Head and Spinal Injuries Centre. Physiotherapy plays an important part in these cases and is carefully planned for each patient as a part of the entire program of treatment. In the early stages of treatment the physiotherapist assists the nursing staff in keeping the paralyzed limbs in proper position to avoid deformities of various types. Permanent fixation of the paralyzed limbs in any one position is avoided. Passive movements of the joints of all paralyzed limbs is also a part of the early treatment; and such movements are continued in the later, spastic stage. In patients admitted to the Centre in the later stages in whom contractures have developed, such passive movements have also proved of value. Electrical stimulation of paralyzed muscles is employed daily, beginning as early after injury as possible, and continued with increasing number of contractions. In the treatment of flexor spasm, regular passive movements, especially if carried out under water in a bath kept at a uniform temperature, have proved of definite value. In addition to passive movements of the paralyzed limbs, active exercises are planned to develop and train the non-paralyzed muscles for compensatory action to improve the balance and mobility of the body. The development and training of the abdominal muscles is of special importance for restoration of bladder function; training of the abdominal and back muscles restores sexual function in patients with low thoracic and cauda equina lesions. Even in injuries to the cervical cord the over-development and training of the few muscles of the upper limbs is of aid in furthering the patient's rehabilitation and independence. For the development and training of muscles, exercises with the aid of suspension in slings and against resistance with pulley and weights are of definite aid; such exercises also are of importance in the restoration of vasomotor control during postural changes; especially in cases with high lesions. While confined to bed and the wheel chair, the patient is trained in dressing himself in a minimum of time and exercises to restore balance. As soon as muscle power in the non-paralyzed muscles and balance of the body have improved sufficiently, walking exercises are begun, first between parallel bars or in walking chairs and later on crutches. To aid in standing and walking, various appliances must be used, chiefly calipers and braces. These should be as light as possible. In most cases pelvic bands and abdominal corsets are not used, as they interfere with the development of proper balance and involve the danger of pressure sores. Only in selected cases, with deformities and over-flexibility of the hip-joints, a pelvic band (or even a corset) may be indicated. Games are an important part of physical therapy and also have a definite psychological value. Certain games, including ball games, can be played while patients are still confined to bed; they provide good exercise for shoulder and trunk muscles. The author has devised a special form of polo played in wheel chairs, which exercises the whole upper part of the body and promotes improved circulation. Physical therapy is supplemented by occupational therapy and training for employment in industry, as well as by cultural entertainment and recreation, in which music plays an important part. The results of these various measures have been "most encouraging" in the rehabilitation of paraplegics.

Comments

The author discusses the value of the various aspects of physical medicine in the rehabilitation of 160 traumatic paraplegics at the Ministry of Pensions Hospital at Stoke Mandeville, England. He stresses the need for teamwork among all those concerned in the treatment, from the earliest moment after injury, giving as the two fundamenals, "an early start and continuation". The two main groups embodying the aims of physical medicine are (a) prevention of contractures and atrophy in the paralyzed parts and (b) adaptation therapy of normal parts of the body (compensatory training).

The worst contractures were found in those

who had lain in fracture beds for months—it took months and years of hard work to remedy or at least diminish the damage done.

Dressing exercises help to adjust the paraplegic to postural changes whilst in bed and to prepare him for future independence. He is taught to get into his clothes and into his wheel chair in the least possible time. With a complete lesion of the 11th thoracic segment, causing complete paraplegia and sensory loss, one patient made the grade in 4 minutes. He had on a pair of shorts only to begin, to which he added a shirt, a tie, 2 pairs of trousers, socks, jacket and shoes and hoisted himself into his wheel chair. Higher cord lesions, or lower ones with severe reflex spasms or marked stiffness, will call for more time, but even those with 3d thoracic lesions, after regular practice, can accomplish the task in 15 minutes.

As quickly as possible, in some complete transverse lesions as early as 5 to 8 weeks after injury, promotion to a wheelchair is in order. Where abdominal and trunk muscles are paralyzed, special exercises, raising the arms in all directions, in front of a mirror, are given for balance. Walking to music is encouraged. Patients with lesions at the 12th thoracic segment with complete paralysis of both lower limbs and sensory loss below the 12th thoracic and 1st lumbar segments have been trained to walk 250 yards in 13½ to 16 minutes on elbow crutches.

Examination for pressure on insensitive spots to prevent bedsores is most important as they are extremely slow in healing.

Occupational therapy and work therapy are added to physical therapy as soon as possible, so as further to increase the patient's future independence.

If patients desire to remain in sheltered conditions, whether married or unmarried, the Ministry of Pensions promises to establish such retreats so as to free them from the restrictions and prejudices of so-called normal people. Those able to go to work can go out daily in their wheelchairs.

In this country there were 2500 cases of spinal injury at the close of World War II. It is due to the early treatment by internist, surgeon, urologist, neurosurgeon, psychiatrist, with good nursing care, and the early skilled use of physical measures as an adjuvant to the skills of previous workers, that most of these are alive and able to take their places in the world.

In World War I these cases died because there was not the team work, the early treatment, the advances in neurosurgery, the amount of nursing care, the psychiatry, and, certainly, physical measures were not considered of much value by most military leaders, who knew little or nothing about them and cared less.

There were then, as now, outstanding workers in Physical Medicine who daily were restoring civilians to life and work and who were only too anxious to help the war wounded, but their aid was spurned until late in the war and then only after all other measures had been used and recovery was delayed and crippling and/or death were inevitable.

By the Vocational Training Act of 1920, rehabilitation was predicated on the man's handicap and his training centered around it. By the Act of 1943, any person in any way connected with the war, or on a pay roll, is entitled to as complete physical restoration as possible and then vocational training to fit him for a job. So there is no excuse for the wage earner not to be reconditioned if he has been neglected through some oversight or his own stubbornness. Unfortunately, domestic workers, housewives, handicapped and crippled children are "the lost people" in this program and they, too, should be taken thought of, if for no other reason than to save enormous taxes due to the burden of their support. Hospitals with half empty clinics could well take these in hand instead of catering to the well-to-do posing as paupers, who clutter the various outpatient departments and prevent these handicapped ones from receiving the treatment that is their due. ***M.C.L.McG.***

Effects of Elevated Body Temperature on the Plasma Ascorbic Acid

R. M. Craig and associates (*Archives of Physical Medicine,* 27:603, Oct. 1946) report a study of the effects of fever therapy on the plasma ascorbic acid level in 58 patients. If it should be found that fever therapy causes a definite decrease in plasma ascorbic acid, this would indicate that care should be taken to maintain the ascorbic acid balance in patients undergoing this type of therapy. Determinations of the plasma ascorbic acid before instituting therapy showed that in the great majority of the 58 patients studied the plasma ascorbic acid values were "extremely low." In the first 29 patients, given the hospital diet for three or four days and a glass of fruit juice in the morning before being placed in the fever cabinet, the plasma ascorbic acid values were raised somewhat, but still remained low. The other 29 patients were given supplements of ascorbic acid in tablet form for one to three days before fever therapy was begun, which resulted in an increase in the ascorbic acid level in the plasma. Fever therapy in the first group consisted of

elevation of the body temperature to 105° or 106°F. for three, six to eight hours; this was combined with chemotherapy with mapharsen, bismuth or sulfathiazole. In the second group, the temperature was maintained at 106°F. for six hours; penicillin was given intramuscularly. There was no significant decrease in the plasma ascorbic acid values in either group.

Comment

Research workers have not yet agreed among themselves as to vitamin C requirements for health, prevention of scury, etc. Clinicians are usually insistent upon its value.

In bronchopneumonia following prostatectomy, Dr. Slotkin of Buffalo and Lt. R. S. Fletcher, M.C., A.U.S., say that 25 mg. of ascorbic acid, 4 times daily, may be life saving. Tonicity of the capillaries is increased, no more fluid leaks into the lung and what is there is soon absorbed.

The patient receiving hyperthermy up to 105° F., 105.5 to 106° F. is undergoing an ordeal equal to several operations and needs all the help possible to tide him ovr. Citrus fruit drinks are usually stressed before, during and after fever, so there should be a safe margin, depending on the condition of the patient.

Some arsenicals and sulfonamides do affect the ascorbic acid metabolism and when these are given in conjunction with fever, theoretically there might be a change in the blood level. Therefore, it might be well to supplement that which is present by adding ascorbic acid in greater quantity than usual.

These experiments were made at the Chicago Intensive Treatment Center for Venereal Diseases under Direction of Dr. Herman N. Bundesen, Commissioner of Health, by Drs. Craig, Schwemlein, Kendall, Farmer and Aron. They found no marked loss of ascorbic acid in patients already low, after 3 to 8 hours of fever from 105 to 106°F. On the other hand, Daum, Boyd and Paul and Falke report a definite and regular decrease in the plasma content after hyperthermy. M.C.L.McG.

Influence of Duration and Frequency of Treatment in Electrical Stimulation of Paralyzed Muscle

A. J. Kosman, S. L. Osborne and A. C. Ivy (*Archives of Physical Medicine*, 28:12, Jan. 1947) report experiments on rats in which the gastrocnemius muscles were denervated by section of the sciatic nerve bilaterally, and the muscle on one side stimulated with a modulated alternating current with a carrier frequency of 25 cycles per second. In previous experiments on rats this type of alternating current had been found to be the most effective in preventing muscle atrophy. In the present experiments it was found that brief periods of stimulating (30 seconds) were as effective as longer periods (15 minutes) in retarding denervation atrophy. Increasing the number of daily electrical stimulation treatments to three increased the effectiveness of the treatment for the prevention of denervation atrophy; but increasing the number of daily treatments to six did not result in any further improvement. The fact that short and long treatment periods were equally effective in experiments on rats is due to the fact that rat muscle fatigues rapidly. It was found that when electrical stimulation was applied three times daily to the denervated muscle with two, five, or ten minutes rests between stimulations, there was definite benefit from the multiple stimulations only in the muscles rested for ten minutes. In applying these experimental results to the clinical use of electrical stimulation for paralyzed muscles, it was found that in man alternating current with a carrier frequency of 5 to 25 cycles produces strong contractions in paralyzed muscles without causing the patient much discomfort. As indicated by the animal experiments, stimulation after the muscle shows fatigue is not indicated. Treatments should be given daily with brief periods of stimulation and rest, and this can be done in the time that the patient usually spends in the clinic. This procedure has given excellent results, especially in those cases in which the stimulation of several muscles in the same patient is necessary.

Comment

This paper should be in the hands of those who first see peripheral nerve injuries. In these experiments, treatment was begun the day after section of the nerve. Rarely, among humans with peripheral nerve paralysis, is the patient sent for treatment until 10 to 21 or more days after the injury when the denervated muscles are atrophied, stiff and fixed. Long and repeated sessions will be required in such cases.

When a Bell's palsy is sent as soon as discovered the gentlest of warmth, mild continuous galvanic treatment with several quick motor point stimulations, later on the sine

wave, followed by massage and exercise will effect rather rapid recovery. Too long a treatment may induce fatigue, too strong a treatment may "set" the muscles and delay recovery. The patient's tissue tolerance is the best guide for treatment.

The longer the delay in treatment and the greater the nerve degeneration, the longer it takes for recovery and, frequently, some deformity persists. Early diagnosis and early treatment means early recovery.

In postoperative and postpartum brachial or radial paralyses, where cases are more likely to be sent early, daily or twice daily treatments soon have the patient using the arm and hand and helping considerably to overcome the deformity.

The neurologist's idea is to wait until inflammation subsides, the physiatrist's aim is to lessen the inflammation and keep the muscle toned up until the nerve recovers and takes over. The patient is worried, anxious, tense until his face or other part recovers and even then he fears it is not as it was or that the condition may recur. ***M.C.L.McG.***

CANCER

—concluded from page 303

five with Lobectomy; four with Diathermy and X-ray; six with Diathermy, radium and X-ray; six with Diathermy and radium; three with X-ray; three with Diathermy; two with no treatment.

There have been three postoperative deaths (7.8 per cent).

Twelve of the patients survived for more than one year after treatment: three, two years; one, three years; three, four years; one, four and one half years; one, five years; one, six years; one, eight years; and one, twelve years. The patient who survived twelve years was treated with x-ray alone.

A lung tumor may, histologically, seem to be benign; but what would be the final outcome if such a tumor remained in the body of a living patient? If such a growth is in a laboratory it cannot become carcinomatous.

N. Y. U. College of Medicine Goes on the Air

New York University College of Medicine, in cooperation with WNBC, New York, has inaugurated a series of weekly programs entitled "How's Your Health?", featuring members of the faculty as guest speakers and Dean Currier McEwen as "medical moderator." The program, heard every Saturday afternoon from 2 to 2.15, originates from Dean McEwen's office at the College of Medicine.

Baruch Committee on Physical Medicine Reports

Increased opportunities in rehabilitation for the 23,000,000 Americans disabled by accident, disease, maladjustment and war are forecast in the annual report of the Baruch Committee on Physical Medicine. The advancements in physical medicine and rehabilitation in the period covered by the report are termed of real significance in medical history by the Committee, composed of leading physicians and medical educators.

Medical BOOK NEWS

Edited by
ALFRED E. SHIPLEY, M.D., Dr. P.H.

All books for review and communications concerning Book News should be addressed to the Editor of this department, 1313 Bedford Avenue, Brooklyn 16, N. Y.

Classical Quotations

● While working with staphylococcus variants a number of culture-plates were set aside on the laboratory bench and examined from time to time. In the examinations these plates were necessarily exposed to the air and they became contaminated with various micro-organisms. It was noticed that around a large colony of a contaminating mould the staphylococcus colonies became transparent and were obviously undergoing lysis. . . It was found that broth in which the mould had been grown at room temperature for one or two weeks had acquired marked inhibitory, bactericidal and bacteriolytic properties to many of the more common pathogenic bacteria.

ALEXANDER FLEMING, F.R.C.S.
Brit. J. of Exper. Path. 10:226 (June) 1929.

Nurses in War

Navy Nurse. By Page Cooper. New York, McGraw-Hill, [c. 1946]. 8vo. 226 pages, illustrated. Cloth, $2.50.

THIS book is written in a very interesting style and gives a clear picture of the exciting experiences which occurred during World War II. It should be very fascinating to the average person and it pays a great deal of tribute to nurses.

The rehabilitation work done for the men in the service is pictured and shows how vital this is for sound minds and bodies for our returning veterans.

The book is well written and the pictures show good photography and are educational.

MARIE M. BEHLEN

Cantor

Ambulatory Proctology. By Alfred J. Cantor, M.D. New York, Paul B. Hoeber, [c. 1946]. 8vo. 524 pages, illustrated. Cloth, $8.00.

UNFORTUNATELY the author's denition of *Ambulatory Proctology* is so spectacular that it weakens his entire purpose and effort:—

"Ambulatory proctology is the diagnosis and treatment of diseases of the anus, rectum, and sigmoid bowel without confining the patient to bed. The treatment may be medical or surgical, conservative or radical. If the patient is not confined to bed that treatment must be defined as ambulatory. Thus, if a proctologist excises a pilonidal cyst, performs an extensive hemorrhoidectomy, or amputates a rectal prolapse, and then returns that patient to his home, although not necessarily to bed, that case has been treated by ambulatory proctology."

In addition to stressing office surgery and sending the patient home although not necessarily to bed, this volume contains the information usually found in recent books on diseases of the anus, rectum, and colon. Included in the illustrations are two photographic reproductions of the author using the telescopic sigmoidoscope which he devised.

If any harm could come from the publication of such a book, it would be that incompetent individuals might be encouraged to attempt "ambulatory proctology."

A. W. MARTIN MARINO

For the Lay Reader

New Worlds in Medicine. An Anthology. Edited with commentary and introduction by Harold Ward. New York, Robert M. McBride, [c. 1946]. 8vo. 707 pages, illustrated. Cloth, $5.00.

This anthology of carefully selected subjects falls into two categories, technical and social, and covers such contemporaneous subjects as cancer, geriatrics, endocrinology, psychosomatics, etc.

It might well be recommended to one's more intelligent patients as an educational medium in promoting better understanding and relations between the medical profession and society.

J. J. WITTMER

Annual of Neurology and Psychiatry

Progress in Neurology and Psychiatry. An Annual Review. 1946. Edited by E. A. Spiegel, M.D. New York, Grune & Stratton, [c. 1946]. 8vo. 708 pages. Cloth, $8.00.

This publication serves a practical need in helping physicians keep abreast of recent advances. It is not intended to replace existing abstract services, but rather to amplify them through selected surveys.

It might be desirable in succeeding issues to have a larger space devoted to psychiatry, which now ranks as number one public health and medical challenge.

FREDERICK L. PATRY

Personality Disorders

Current Therapies of Personality Disorders. The Proceedings of the 34th Annual Meeting of the American Psychopathological Association, held in New York City, April, 1945. Edited by Bernard Glueck, M.D. New York, Grune & Stratton, [c. 1946]. 8vo. 296 pages. Cloth, $3.50.

This book gives a picture of the present day status of psychiatric practice in many of its aspects and especially in relation to the changing attitudes, policies and technics resulting from the larger application of psychiatry in human relationships during the war years.

C. MILTON MEEKS

Blood

Principles of Hematology. By Russell L. Haden, M.D. 3rd Edition. Philadelphia, Lea & Febiger, [c. 1946]. 8vo. 366 pages, illustrated. Cloth, $5.00.

This is a concise and well presented booklet on the physiologic and the pathologic conditions of the blood. The usual laboratory procedures are discussed clearly and from a practical point of view. The author shows unusual power and ability to make this otherwise dry subject extremely interesting.

HARRY APFEL

Medical Care

Medicine in the Changing Order. Report of the New York Academy of Medicine Committee on Medicine and the Changing Order, Malcolm Goodridge, M.D., Chairman, New York, Commonwealth Fund, [c. 1947]. 8vo. 240 pages. Cloth, $2.00.

This is an excellent report on the evolution of the practice of medicine in this country as a whole, going back to the 19th century and leading up to the present time. The many suggestions and possible solutions for the changing order demand careful study.

J. J. WITTMER

Physiological Chemistry

Lehrbuch der Physiologischen Chemie. By Professor Emil Abderhalden. 23|25 Edition. Basel, Switzerland, Benno Schwabe & Co., [c. 1946]. 8vo. 417 pages, illustrated. Cloth, 26 Fr.

This text gives a complete presentation of our current knowledge of physiological chemistry. The completeness and the excellent presentation in spite of the shortness make the book a masterpiece. It is highly recommended to students and physicians interested in physiological chemistry and its clinical applications.

MAX G. BERLINER

Breast Pathology

Diseases of the Breast. Diagnosis. Pathology. Treatment. By Lt. Commdr. Charles F. Geschickter, M.C., U.S.N.R. With a Special Section on Treatment in Collaboration with Murray M. Copeland, M.D. 2nd Edition. Philadelphia, J. B. Lippincott Co., [c. 1945]. 8vo. 826 pages, illustrated. Cloth, $12.00.

This work is based upon the experience of outstanding men at Johns Hopkins Hospital. Their case histories, specimens, and follow-up studies are tabulated so that the reader may draw definite conclusions concerning various diseases of the breast.

The book is highly recommended to all interested in breast pathology.

MERRILL N. FOOTE

Retinal Diseases

Diseases of the Retina. By Herman Elwyn, M.D. Philadelphia, Blakiston Company, [c. 1946]. 8vo. 587 pages, illustrated. Cloth, $10.00.

THIS book is well indexed and well illustrated. It covers retinal diseases due to disturbances of circulation, malformations, degenerative diseases on a hereditary basis, retinal inflammations, tumors, diseases leading to detachment, developmental anomalies, and radiation effects. The author has done an excellent piece of work and the publishers have done their part in full. The student in ophthalmology will find it of greatest benefit and the practitioner will find it helpful for his preliminary survey, and with the adequate bibliography appended to each section, can widen his field as he will. Many retinal conditions offer little hope of improvement as the damage is already done but no field in medicine should be negletced. If this policy had not been followed, retinal detachment would be as of 25 years ago with a recovery rate of zero.

RALPH I. LLOYD

Anatomy for the Layman

The Romance of Human Architecture. By Maurice Chideckel, M.D. Boston, Bruce Humphries, [c. 1945]. 8vo. 107 pages. Cloth, $2.00.

IN approximately one hundred pages the author attempts to summarize most of the anatomy and physiology of the human body in a manner which is intended to clarify "the perplexing questions" about the problems "that the flesh is heir to." It would appear that this volume is intended for the layman. If it is so intended, the layman would be required to have some advance knowledge. For each sentence is so full of statements that it would require careful study. In an attempt at simplicity, a good many misleading generalities are stated.

This book would have little value for the physician. It is also difficult to decide what group of laymen would be benefited by it. It is too simplified for the doctor, and too detailed for the average reader. Such an impression is unfortunate, for the author has undoubtedly given much thought and effort to this little book.

VICTOR GROVER

Food and Energy

Bioenergetics and Growth. With Special Reference to the Efficiency Complex in Domestic Animals. By Samuel Brody, Ph.D. New York, Reinhold Pub. Co., [c. 1945]. 8vo. 1,023 pages, illustraed. Cloth, $8.50.

THIS very interesting book is not written by an M.D. It is a research compilation by an investigator in agricultural chemical research at a College of Agriculture. It deals primarily with energy production in animals in relation to the efficiency of agricultural processes in the production of meat, milk, eggs, wool, etc. It considers the various factors which affect the efficiencies of such production and the translation into energy. This volume touches on fundamental processes well known to the clinician but posited far back beyond the point at which the clinician's concepts originate, namely the very production of the foods, etc. themselves and a mathematical relation to the efficiency of production of muscular work in animals. Specific dynamic action of foods, planes of nutrition, reproduction, and growth in animals are carefully appraised. The nutritionist should find this a rather novel approach to truths which he has long since accepted. *Bioenergetics* is in the review's opinion a very descriptive and apt title.

GEORGE E. ANDERSON

Venous Pulse

The Venous Pulse and Its Graphic Recording. By Franz M. Groedel, M.D. New York, Brooklyn Medical Press, [c. 1946]. 4to. 223 pages, illustrated. Cloth, $5.50.

THIS book attests to a great amount of work done in the study of the venous pulse. The author goes back into the past and quotes authors whose conclusions are no longer valid and does this so often that a confused presentation of the subject results. There is still too much uncertainty as to the meaning of the waves of the phlebogram to make phlebography of value to the clinician. When it comes to the concussion waves superimposed, they are hardly understood at all. The pneumocardiograph and the esophago-cardiograph are ingenious methods for the study of

NEW BOOKS AND NEW EDITIONS

FOR FALL PUBLICATION

GRANT: Atlas of Anatomy — 2nd edition

By J. C. BOILEAU GRANT, Professor of Anatomy, University of Toronto. *8½ x 11, 546 pp., 591 plates* $10.00

The accuracy and artistic perfection of the plates in the Atlas have from the first evoked the praise of physicians and teachers everywhere. The regional presentation is carefully adapted to modern teaching methods, and the original illustrations include many views not found in other atlases. The present edition gains in value through the additional use of color and a more convenient arrangement. Illlustrations have been added to fill gaps or to demonstrate more adequately certain sections.

PARKER: Textbook of Clinical Pathology — 3rd edition

Edited by FRANCIS P. PARKER, M.D., University of Virginia. *6 x 9, 780 pp., 229 figs., 46 plates* $6.00

Because of the pressure of other duties, Dr. Roy Kracke, former chief editor, found it necessary to withdraw from the work for this third edition. The revision, however, in the capable hands of Dr. Parker, is complete—in fact, the book has been almost entirely rewritten. Changes include the bringing up to date of material from former editions and the addition of new procedures developed in the last six years. Rearrangement of sequence in some sections has improved the continuity of the text.

WHITE and WEINSTEIN: Blood Derivatives and Substitutes

By CHARLES STANLEY WHITE, M. D., Chief of Surgery, Doctors Hospital, Washington, D. C.; and JACOB JOSEPH WEINSTEIN, M. D., Associate in Surgery, George Washington University School of Medicine. *6 x 9, 530 pp., 196 figs.* $7.50

The authors present a comprehensive study of plasma and plasma substitutes and by-products, with the chief emphasis on the practical and clinical viewpoints. The chemical and physiological aspects of blood, plasma and plasma substitutes are stressed, and similarly their preparation, storage and administration are described in detail. An entire section is devoted to an important discussion of shock and its treatment.

WALSH: Clinical Neuro-ophthalmology

By FRANK B. WALSH, M.D., Wilmer Clinic, Johns Hopkins Hospital. *6⅞ x 10, 1448 pp., 384 figs.* $15.00

Dr. Walsh has worked for many years on clinical diagnosis with colleagues in several departments of the Johns Hopkins Hospital and the Baltimore City Hospitals. The material in his book is based on this long and varied experience. Complete coverage is given. The necessary anatomic, physiologic, neurologic and other basic information is included in the text where it seems indicated. Numerous case histories illustrate the variability of cases and present the problems in differential diagnosis.

THE WILLIAMS & WILKINS COMPANY

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pressure changes within the thorax and the effect of the motions of the heart upon them. As yet, the technical difficulties appear too great to make these methods reliable.

The author makes a good plea for further study in the field of phlebography and expresses the hope that, as a result, the method will become of value clinically.

EDWIN P. MAYNARD, JR.

Man Midwife

With Cradle and Clock. By Knud Stowman. New York, Harper & Bros., [c. 1946]. 8vo. 292 pages. Cloth, $2.50.

THIS novel is historical in that it depicts New York in its early infancy. It is the story of America's first obstetrician. It is factual as to the period and the characters presented. A young doctor sets himself the task of breaking down the prejudice and ridicule of the populace against a man-midwife. How he succeeded makes most interesting reading. How he won the love of an older physician's daughter and the confidence of the common people injects both romance and science into the picture.

This book should not be passed up by the obstetrician nor by any doctor interested in the history of medicine in America.

THOMAS B. WOOD

Short Obstetrics and Gynecology

Synopsis of Obstetrics and Gynaecology. By Aleck W. Bourne, M.D. 9th Edition. Baltimore, Williams & Wilkins Co., [c. 1945]. 12mo. 500 pages, illustrated. Cloth, $5.00.

AS the title indicates this work is purely a synopsis of obstetrics and gynecology. The author has adhered strictly to a presentation of known facts, offered without discussion, in a more or less tabulated form. There is no elaboration, and controversy is carefully avoided. The book provides an excellent basis for the study of its subject matter by the undergraduate and may well be a valuable source of information to the qualified doctor.

WILLIAM C. MEAGHER

BOOKS RECEIVED

for review are promptly acknowledged in this column: we assume no other obligation in return for the courtesy of those sending us the same. In most cases, review notices will be promptly published shortly after acknowledgment of receipt has been made in this column.

Vitamine, Hormone, Fermente. Ein Buch fur Arzte, Biologen und Studierende. By Dr. Rudolf Abderhalden. 3rd Edition. Basel, Switzerland, Benno Schwabe & Co., [c. 1946]. 8vo. 250 pages, illustrated. Cloth, 14.50 fr.

Henry Sewall. Physiologist and Physician. By Gerald B. Webb & Desmond Powell. Baltimore, Johns Hopkins Press, [c. 1946]. 8vo. 191 pages, illustrated. Cloth, $2.75.

Mussolini e Hitler. Dal Punto di Vista Psichiatrico. By Dr. Tommaso Senise. Naples, Biblioteca di "Il Cervello," [1947]. 8vo. 64 pages. Paper.

The Ego and the Mechanisms of Defence. By Anna Freud. Translated from the German by Cecil Baines. New York, International Universities Press, [c. 1946]. 8vo. 196 pages. Cloth, $4.00.

Gastroenterology in General Practice. By Louis Pelner, M.D. With the collaboration of Louis A. Held, M.D., and contributions from Alexander Lewitan, M.D., Samuel Waldman, M.D., & Siegfried W. Westing, M.D. Springfield, Ill., Charles C. Thomas, [c. 1946]. 8vo, large. 285 pages, illustrated. Cloth, $7.50.

Allergy in Theory and Practice. By Robert A. Cooke, M.D. In Association with Horace S. Baldwin, M.D., Robert Chobot, M.D., R. Clark Grove, M.D., and others. Philadelphia, W. B. Saunders Co., [c. 1947]. 8vo. 572 pages, illustrated. Cloth, $8.00.

The Story of Human Birth. By Alan Frank Guttmacher, M.D. Revised Edition of INTO THIS UNIVERSE: THE STORY OF HUMAN BIRTH. New York, Penguin Books, [c. 1947]. 16mo. 214 pages, illustrated. Board, 25c.

Medicine in the Changing Order. Report of the New York Academy of Medicine Committee on Medicine and the Changing Order, Malcolm Goodridge, M.D., Chairman, New York, Commonwealth Fund, [c. 1947]. 8vo. 240 pages. Cloth, $2.00.